"A STUDY ON CORRELATION BETWEEN ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST"

Dissertation Submitted to

THE TAMILNADU Dr. MGR MEDICAL UNIVERSITY

Chennai-600 032

In partial fulfillment of the regulations for the Award of the degree of

M.S. (General Surgery)

Branch – I

MADRAS MEDICAL COLLEGE

CHENNAI

MAY - 2019

CERTIFICATE

This is to certify that, the dissertation entitled **"A STUDY ON CORRELATION BETWEEN ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST"**

Is the bonafide work done by **DR.M.HARINI,** during his **M.S. (General Surgery)** course2016-**2019**, done under my supervision and is submitted in partial fulfillment of the requirement for the M.S. (BRANCH-I) - General Surgery of The TamilnaduDr.MGR Medical University, May 2019 examination.

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DECLARATION

I solemnly declare that this dissertation **"A STUDY ON CORRELATION BETWEEN ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST"** was prepared by me at Institute of General surgery, madras medical college and RAJIV GHANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI under the guidance and supervision of **PROF.M.ALLI.M.S.,D.G.O,** professor of general surgery, institute of general surgery,madras medical college, Chennai. This dissertation is submitted to the Tamil Nadu DR.MGR Medical University, Chennai in fulfillment of the university regulation for the award of the degree M.S.General Surgery (branch 1).

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ETHICAL COMMITTEE APPROVAL

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To

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Dear Dr.M.Harini,

The Institutional Ethics Committee has considered your request and approved your study titled "**A STUDY ON CORRELATION BETWEEN ER, PR, HER-2/NEU STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST" - NO.08062017(A)**

The following members of Ethics Committee were present in the meeting hold on **20.06.2017** conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD.,	:Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., MMC,Ch-3	: Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
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5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC	: Member
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7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3	: Member
8.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
9.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist
10.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
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LIST OF ABBREVATIONS

CA	–	carcinoma breast
ER	–	Estrogen receptor
PR	–	Progesterone receptor
HER 2 NEU	–	Human epidermal growth factor receptor - 2
LVI	–	Lymphovascular invasion
BMI	–	Body mass index
NP	–	Nodal positivity
TS	–	Tumour size
AN	–	Axillary node
FNAC	–	Fine needle aspiration cytology
EBC	–	Early breast carcinoma
LABC	–	Locally advanced carcinoma
BCS	–	Breast conservation surgery
MRM	–	Modified radical mastectomy
NACT	-	Neoadjuvant chemotherapy
RT	-	Radiotherapy

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ABSTRACT

INTRODUCTION:

Breast cancer is now the most common cancer in woman .There are several factors which influence the development of breast malignancies such as the genetic background, reproductive parameters and the consequences of female hormones both intrinsic and extrinsic. Numerous studies have examined prognostic factors for survival of breast cancer patients, but relatively few have dealt specifically with relationship between hormonal receptor status, BMI and lymphovascular invasion.

AIM AND OBJECTIVES:

To study the correlation between hormonal receptors status (ER, PR, HER 2 NEU) and other prognostic factors like age, node, BMI, menopausal status, lymphovascular invasion in carcinoma breast

METHODOLOGY:

All patients who fulfill the inclusion criteria were included in the study after obtaining written informed consents. Patient age, body mass index, tumour size, node, menopausal status is noted. The histopathology, ER, PR and HER-2/neu receptor status and lymphovascular invasion are obtained from trucut biopsy and specimen. The correlation of these prognostic factors was observed in our study.

RESULTS:

The mean age of carcinoma of breast was 48.5 years of age in our study. Positive receptor status(ER, PR & BOTH ER& PR) is strongly associated with normal BMI and decreased lymphovascular invasion. Negative receptor status(ER, PR & BOTH ER& PR) is strongly associated with obese patients and increased lymphovascular invasion in carcinoma breast.Normal BMI is associated with decreased lymphovascular invasion and obese BMI patients are associated with increased lymphovascular invasion in both pre and post-menopausal women. HER 2 NEU receptor status and node have no significant association with lympho vascular invasion and body mass index.

INTRODUCTION

INTRODUCTION

Carcinoma breast is one of the most common carcinoma occurring in females. It is a major illness that affects the female physically and mentally. In India, it is the leading cancer among women. Chennai ranks third (32.6) among Indian states. India has the highest number of breast cancer deaths in the world (70218) followed by China (47984) and USA (43909).

The final outcome in breast cancer management depends upon various prognostic factors

- Age
- Tumour size
- Lymph nodes
- Receptor status
- Lymphovascular invasion
- Body mass index

Early diagnosis and treatment will decrease the morbidity and mortality of the disease significantly. The treatment depends upon the patient at which stage they are presenting to the health services. The breast cancer management requires a multi-modality approach, which includes surgery, radiotherapy, chemotherapy, hormonal therapy.

In this study, we planned to study the correlation of the various prognostic factors such as age, BMI, receptor status, node and lymphovascular invasion in patients with carcinoma of breast.

AIMS AND OBJECTIVE

AIMS AND OBJECTIVES

- To evaluate the correlation of prognostic factors such as age, Body mass index,ER, PR HER 2 receptor status in patients with carcinoma of breast

- To study the correlation between hormonal receptors status and other prognostic factors with lymphovascular invasion in carcinoma breast

REVIEW OF LITERATURE

REVIEW OF LITERATURE

ANATOMY OF THE BREAST:

The breast is a modified sweat gland. In 7th week of intrauterinelife, they are derived from the ectodermal milk lines bilaterally. Breast is an accessory reproductiveorgan. They are made of glandular tissue containing 15 to 20lobes. Each lobe is made up of group of alveoli and it is drained by lactiferousduct. Each duct has a dilatation called lactiferous sinusat its termination beneath thenipple. Group of alveoli draining intoduct is called Primary secretory unit. Myoepithelium is a single layer of epithelial cells surrounds only the ducts not lining thelobules. They are contractile and aid the transport of secretions along the duct. Major part of thegland has fatty stroma.

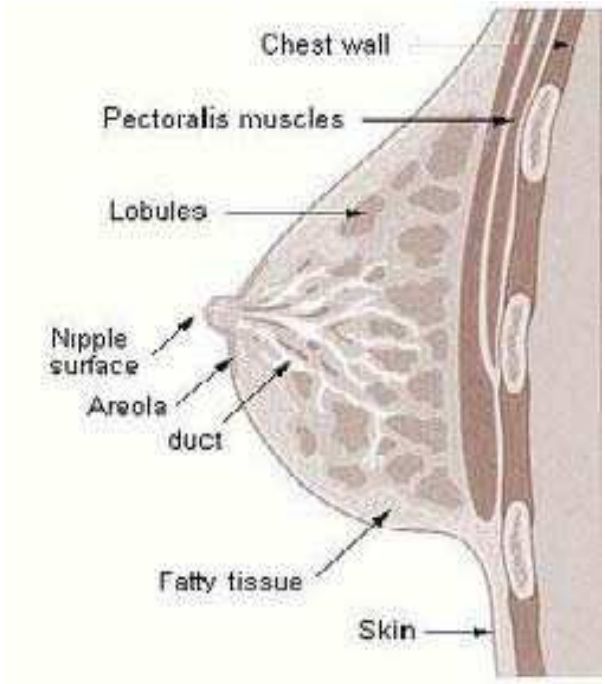


Fig 1: Anatomy of breast

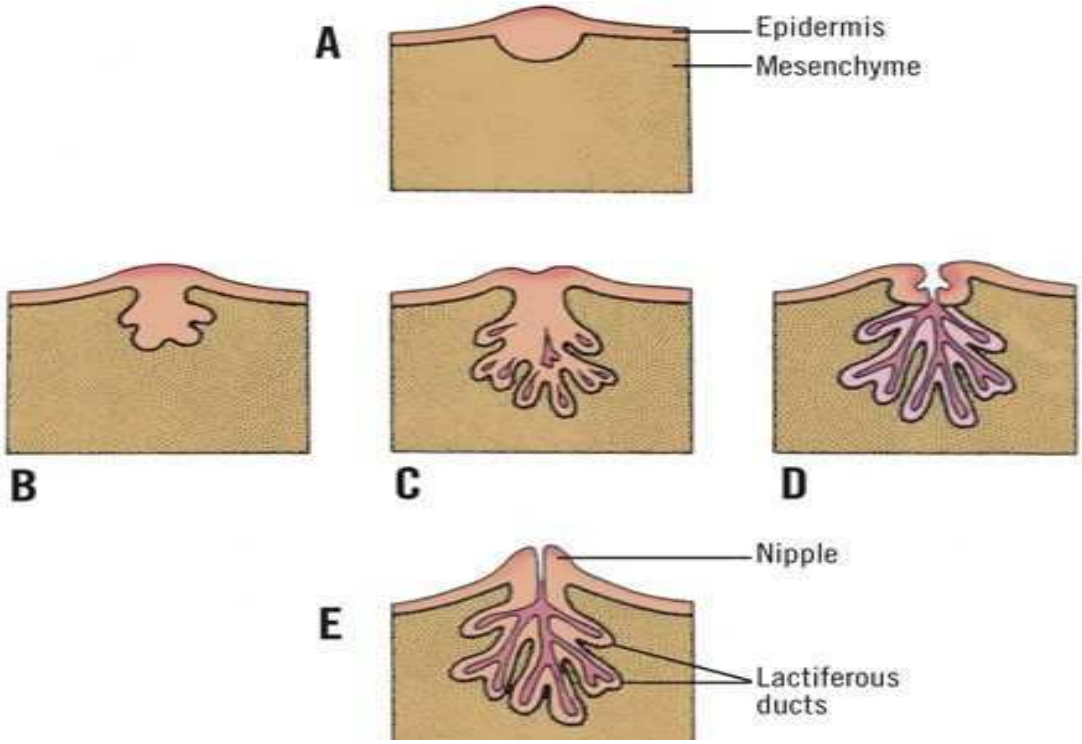


Fig: 2 Development of breast

Plane:

The breast lies superficial to the pectoral fascia.

Extent:

Vertically- Second to the sixth rib

Horizontally- the lateral border of the sternum to mid-axillary line lies over the following muscles:

- Pectoralis major
- Serrartusanterior
- External oblique of the abdomen.

Axillary tail of Spence:

Extension of the breast that passes through the foramen of Langer and therefore this part of breast is deep to the fascia. It has direct contact with lymph node.

Ligament of cooper:

Anchored to the overlining skin and to the underlying fascia by bands of these connective tissues.

Nipple:

Nipple is located at the level of fourth intercostal space. It is pierced by 15 to 20 lactiferous ducts which open independently to nipple. The stiffness of nipple mainly due to circular and longitudinal muscles in it.

Areola:

Areola is a circular pigmented area around nipple. They are rich in modified sebaceous glands. They secrete oily lubricant.

Blood supply of the breast:

The breast is rich in vascular supply.

- Internal mammary artery- a branch of subclavianartery
- Lateral thoracic
- Superior thoracic
- Acromiothoracic

Branches of the axillaryartery

- Posterior intercostal arteries

Venous supply:

The veins follow the arteries. Superficial veins drains into the internal thoracic vein whereas the deep veins drains into the internal thoracic, axillary and posterior intercostal veins.

The communication of posterior intercostals veins with the Batson's vertebral venous plexus is the basis of spread of breast malignancy to vertebra and skull base.

Nerve supply:

- Anterior cutaneous branches of the 4th to 6th intercostals nerves
- Lateral cutaneous branches of the 4th to 6th intercostals nerves.
- Sensory fibres to skin
- Autonomic fibres to blood vessels and smooth muscle.

Lymphatic drainage of breast:

Lymph from the breast drains into the following nodes.

❖ Axillary nodes

- Level 1:lateral to pectoralis minor

Includes anterior or pectoralgroup, posterior orsubscapulargroup, lateral or humeralgroup

- Level 2: posterior to pectoralis minor - Centralgroup
- Level 3:medial to pectoralis minor - apical group

- ❖ Internal mammary (parasternal nodes)
    - situated along internal thoracic vessels
- ❖ Interpectoral or rotters nodes: between pectoralis major and minor.
- ❖ Supraclavicularnodes
- ❖ Cephalic(deltopectoral)nodes,
- ❖ Posterior intercostalsnodes
- ❖ Subdiaphragmatic and subperitoneal lymphplexuses.
- ❖ Few lymphatic pierce the pectoral fascia & enter thechest

Pattern of drainage:

- 75% drains into axillary nodes
- 20% drains into internal mammary nodes
- 5% drains into posterior intercostalnodes.

- Among the axillary nodes, the anterior group drains mostly followed by the posterior and apical group.
- The internal mammary nodes drain the lymph from both inner and outer half of breast.
- A plexus of lymph vessels- sub areolar plexus of Sappey is present deep to theareola.
- Lymphatics from the deeper surface of the breast pass through the pectoralis major muscle and the clavipectoral fascia to reach the apical nodes and also to theinternal mammary nodes.

- Lymphatics from the lower and inner quadrants of thebreast crosses the costal margin and pierces the anterior abdominal wall through the upper part of linea Alba and communicate with the subdiaphragmatic and subperitoneal lymph plexuses.

PHYSIOLOGY OF BREAST:

- Estrogen -ductal development
- Progesterone -epithelium and lobular development.
- Prolactin - lactogeneis during late pregnancy and the postpartum period.

Prolactin results in the upregulation of hormone receptors and aids in epithelial development.

Positive and negative feedback mechanisms exercise stringent control of the hormones secreted from the hypothalamus and thepituitary.

Dramatic changes are noted in the female breast changes during various developmental stages in adolescence, pregnancy, lactation and senescence. The complex interactions among the various hormones are responsible for these changes. Imbalances in these hormones result in several conditions both benign and malignant.

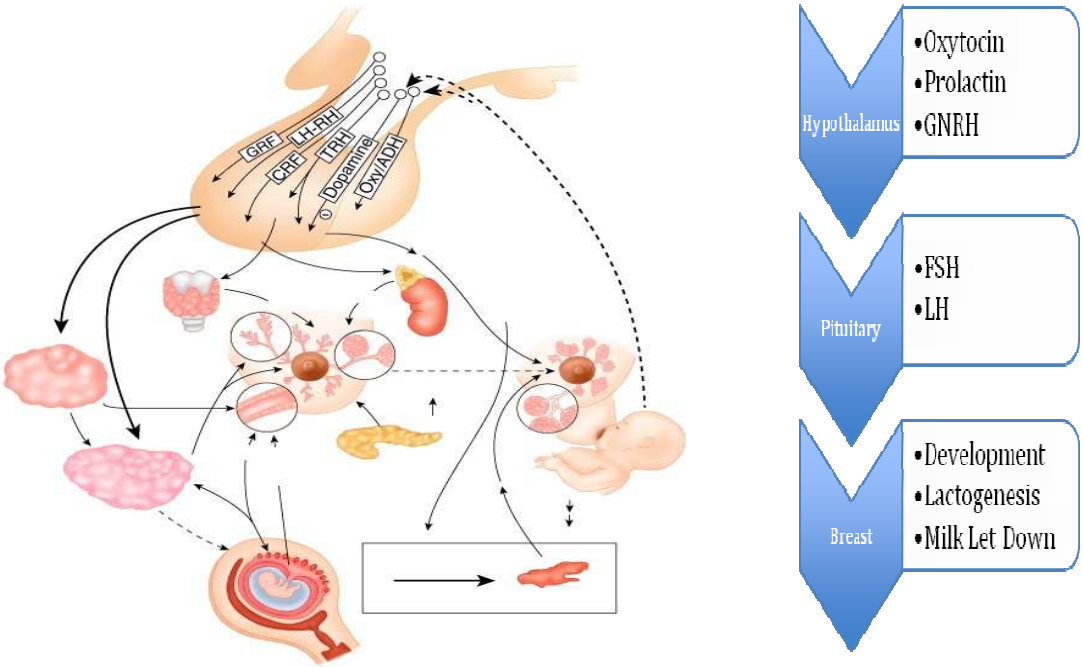


Fig 3: Regulation of Breast Development & Function

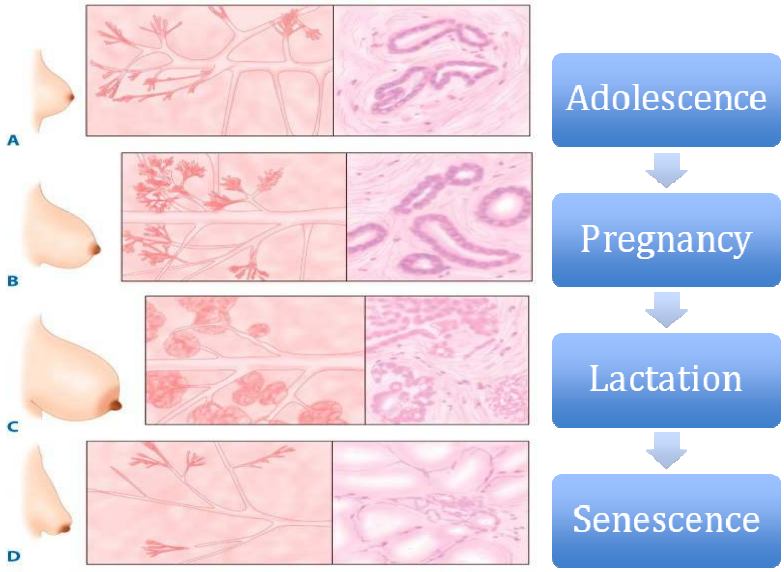


Fig 4: Physiological stages of breast development

CLINICAL PRESENTATION:

Women with carcinoma breast will present with the following complaints:

- Lump in the breast with or without nipple retraction– most common
- An axillary nodemass.
- Symptoms due to metastaticdisease

Liver – abdominal pain / mass / obstructive jaundice

Lung – breathlessnes, cough with hemoptysis, pleural effusion

Bone – pain over long bone site

- Discharge from nipple – rare presentation
- Skin changes:

❖ Paeu d'orange

Is due to cutaneous lymphaticoedema. As the lymphtics are blocked there is lymphatic oedema of the overlying skin and infiltrated skin is tethered by the sweat glands.

It can't swell there by giving an orange peelappearance.

❖ Ulceration

❖ Satellite nodule

RISK FACTOR FOR BREAST CANCER:

Age:

Age is probably the most important risk factor for breast cancerdevelopment. The incidence of breast cancer continues to increase with advancing age of the female population. Breast cancer is rare in women younger than 20 years and constitutes less than 2% of the total cases. Thereafter, the incidence increases to 1 in 233 from ages 30 to 39 years, 1 in 69 from ages 40 to 49, 1 in 42 from ages 50 to 59, 1 in 29 from ages 60 to 69, and 1 in 8 by age 80 years. The women now have an average risk of 12.2% of being diagnosed with breastcancer at some time during their lives.

Sex:

Sex is also an important risk factor because most breast cancers occur in women. Breast cancer also occurs in men. Incidence of breast cancer in men is less than 1% of the incidence in women.

Personal History of Breast Cancer:

The magnitude of risk depends on the age at diagnosis of the first primary cancer, estrogen receptor (ER) status of the first primary cancer and use of adjuvant systemic chemotherapy and endocrine therapy

Histologic Risk Factors:

Histologic abnormalities diagnosed by breast biopsy constitute an important category of breast cancer risk factors. These abnormalities include lobular carcinoma in situ (LCIS) and proliferative changes with atypia. LCIS is an uncommon condition that is observed predominantly in younger

premenopausal women. It is typically an incidental finding at biopsy for another condition and does not manifest as a palpable mass or suspicious microcalcifications on mammography.

HISTOLOGICAL DIAGNOSIS – RR

- Nonproliferative disease - 1.0
- Proliferative disease without atypia 1.3-1.9
- Proliferative disease with atypia 3.7-4.2
- Strong family history 4-9
- LCIS >7

Family History of Breast Cancer and Genetic Risk Factors:

The relationship between family history of breast cancer and the risk for breast cancer is a proven one. First-degree relatives (mothers, sisters, and daughters) of patients with breast cancer have a twofold to threefold excess risk for development of the disease. Risk is much higher if affected first-degree relatives had premenopausal onset and bilateral breast cancer. Risk is not significantly increased in women with distant relatives (cousins, aunts, grandmothers) with breast cancer

GENETIC FACTORS:

Genetic factors are estimated to be responsible for 5% to 10% of all breast cancer cases, but they may account for 25% of cases in women younger than 30 years.

The BRCA1 gene which was identified in chromosome 17(17q21). Mutations in BRCA1account results for 40% of familial breast cancers. The BRCA2 which was identified in chromosome 13 account for 30% of familial carcinoma. In addition to carcinoma breast these patients have additional risk for other carcinoma.

Reproductive Risk Factors:

Reproductive milestones that increase a woman's lifetime estrogen exposure are thought to increase her breast cancer risk. These include

- Onset of menarche before 12 years of age
- First live childbirth after age 30 years
- Nulliparity
- Menopause after age 55 years.

There is a 10% reduction in breast cancer risk for each 2-year delay in menarche; the risk doubles with menopause after age 55. A first full-term pregnancy before age 18 years is associated with half the risk for development of breast cancer of a first full term pregnancy after age 30 years. In contrast to family history or histologic factors, reproductive risk factors have a large influence on breast cancer.

Exogenous hormone use:

Therapeutic or supplemental estrogen and progesterone are taken for various conditions. The two most common reasons are contraception in premenopausal women and HRT in postmenopausal women. Other indications

for use of exogenous hormones include menstrual irregularities, polycystic ovaries, fertilitytreatment, and hormone insufficiency states.

Studies have suggested that breast cancer risk is increased in current or past usersof oral contraceptives but that the risk decreases as the interval after cessation of use increases.

These data show that women receiving combination HRT with estrogen and progesterone for 5 years have approximately a 20% increased risk for the development of breast cancer.

Women who take estrogen-only formulations (because of previous hysterectomy) do not appear to be at increased risk for breast cancer

Non modifiable risk Factors:

- Increasing age
- Female sex
- Menstrual factors
- Early age at menarche (onset of menses before age 12 yr)
- Older age at menopause (onset beyond age 55 yr)
- Nulliparity
- Family history of breast cancer
- Genetic predisposition (BRCA1 and BRCA2 mutation carriers)
- Personal history of breast cancer
- Race, ethnicity (white women have increased risk compared with women of other races) History of radiation exposure

Modifiable risk factors:

- Reproductive factors
- Age at frst live birth (full-term pregnancy after age 30 yr)
- Parity
- Lack of breastfeeding
- Obesity
- Alcohol consumption
- Tobacco smoking
- Use of hormone replacement therapy
- Decreased physical activity
- Shift work (night shifts)

Histologic Risk Factors:

- Proliferative breast disease
- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Lobular carcinoma in situ

STAGING OF CARCINOMA:

Non - invasive Epithelial Cancers

- Lobular carcinoma in situ
- Ductal carcinomain situ or intraductal carcinoma
    - ❖ Papillary
    - ❖ cribriform
    - ❖ solid
    - ❖ comedo

Invasive Epithelial Cancers

Invasive lobular carcinoma (10%)

Invasive ductal carcinoma:

- Invasive ductal carcinoma, not otherwise specifed (50%-70%)
- Tubular carcinoma (2%-3%)
- Mucinous or colloid carcinoma (2%-3%)
- Medullary carcinoma (5%)
- Invasive cribriform carcinoma (1%-3%)
- Invasive papillary carcinoma (1%-2%)
- Adenoid cystic carcinoma (1%)
- Metaplastic carcinoma (1%)

Mixed Connective and Epithelial Tumors:

- Phyllodes tumors, benign and malignant
- Carcinosarcoma
- Angiosarcoma
- Adenocarcinoma

TNM STAGING:

Primary tumour (T):

TX - Primary tumor cannot be assessed

T0 - No evidence of primary tumor

Tis - Carcinoma in situ

Tis (DCIS) DCIS

Tis (LCIS) LCIS

Tis (Paget) Paget disease of the nipple not associated with invasive carcinoma or carcinoma in situ (DCIS and/or LCIS) in underlying breast parenchyma

T1 Tumor ≤ 2 cm in greatest dimension

T1mi Tumor ≤1 mm in greatest dimension

T1a Tumor >1 mm but ≤5 mm in greatest dimension

T1b Tumor >5 mm but ≤10 mm in greatest dimension

T1c Tumor >10 mm but ≤20 mm in greatest dimension

T2 Tumor>2cm but ≤5cm in greatest dimension

T3 Tumor>5cm in greatest dimension

T4 Tumor of any size with direct extension to the chest wall and/or to the skin

T4a Extension to the chest wall, not including only pectoralis muscle adherence or invasion

T4b Ulceration and/or ipsilateral satellite nodules and/or edema of the skin

T4c Both T4a and T4b

T4d Inflammatory carcinoma

Regional Lymph Nodes (N):

Clinical stating

Nx Regional lymph nodes cannot be assessed (e.g., previously removed)

No regional lymph node metastases

N1 Metastases to movable ipsilateral level I, II axillary lymph node(s)

N2 Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases

N2a Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures

N2b Metastases only in clinically detected* ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases

N3 Metastasis in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident

level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

N3a Metastasis in ipsilateral infraclavicular lymph node(s)

N3b Metastasis in ipsilateral internal mammary lymph nodes(s) and axillary lymph node(s)

N3c Metastasis in ipsilateral supraclavicular lymph node(s)

Pathological classification:

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN0 (i-) No regional lymph node metastasis histologically, negative IHC

pN0 (i+) Malignant cells in regional lymph nodes no greater than 0.2 mm

pN0 (mol-) No regional lymph node metastasis histologically, negative molecular findings (IHC)

pN0 (mol+) Positive molecular fndings (RT-PCR), but no metastasis detected by histology or IHC

pN1 Micrometastases; or metastases in 1-3 axillary nodes and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected

pN1mi Micrometastases (>0.2 mm and/or >200 cells but none >2.0 mm)

pN1a Metastases in 1-3 axillary nodes; at least one metastasis >2.0 mm

pN1b Metastases in internal mammary nodes with micrometastasis or macrometastases detected by sentinel lymph node biopsy (not clinically detected)

pN1c Metastases in 1-3 axillary nodes and in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected

pN2 Metastases in 4-9 axillary nodes or in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases.

pN2a Metastases in 4-9 axillary nodes (at least one tumor deposit >2.0 mm)

pN2b Metastases in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases

pN3 Metastases in ≥10 axillary nodes; or in infraclavicular (level III axillary nodes) or in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary nodes; or in >3 axillary lymph nodes and internal mammary lymph nodes, with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected; or in ipsilateral supraclavicular lymph nodes.

Metastasis:

M0 No clinical or radiographic evidence of distant metastases

cM0(i+) No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood,

bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases

M1 distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

TNM stage groupings			
STAGE 0	TIS	N0	M0
Stage IA	T1[a]	N0	M0
Stage IB	T0	N1mi	M0
	T1[a]	N1mi	M0
Stage IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Table 1: Staging of carcinoma breast

PROGNOSTIC FACTORS:

AGE

Age place an important factor in the prognosis of carcinoma breast .Women diagnosed with breast cancer in their early age have a poorer prognosis than women diagnosedinmiddle or olderage. There as on for this unusual pattern is unclear. According to literature breast cancer occurring in younger women is of more aggressive type.

They are usually,

- large size tumour
- Node positivity
- High grade
- Poorly differentiated
- High tumor invasive potential
- Greater chances of early lymphatic spread
- ER,PR negative, Her2 positive

Thus,thepoorer outcome could at least partly be due to differences in these important prognostic factors.Recurrence of the tumour is also more common in younger women than elderly women. In this study we studied the mean age of occurrence of tumour, receptor status at various ages.

OBESITY

Obesity adversely affects women's health.Obesity in women is a recognized risk factor for metabolic syndrome, type II diabetes mellitus, cardiovascular disease and several major cancers including breast and endometrial cancer. The risk of breast cancer increases with obesity and also associated with poor prognosis of breast cancer. Obesity is measured as weight gain, body mass index, waist–hip ratio or percent body fat. In our study obesity is measured in terms of BMI. A one-point gain in BMI is estimated to increase the risk of postmenopausal breast cancer by 3%.There are several mechanisms by which body weight and obesity affect the prognosis of breast cancer.

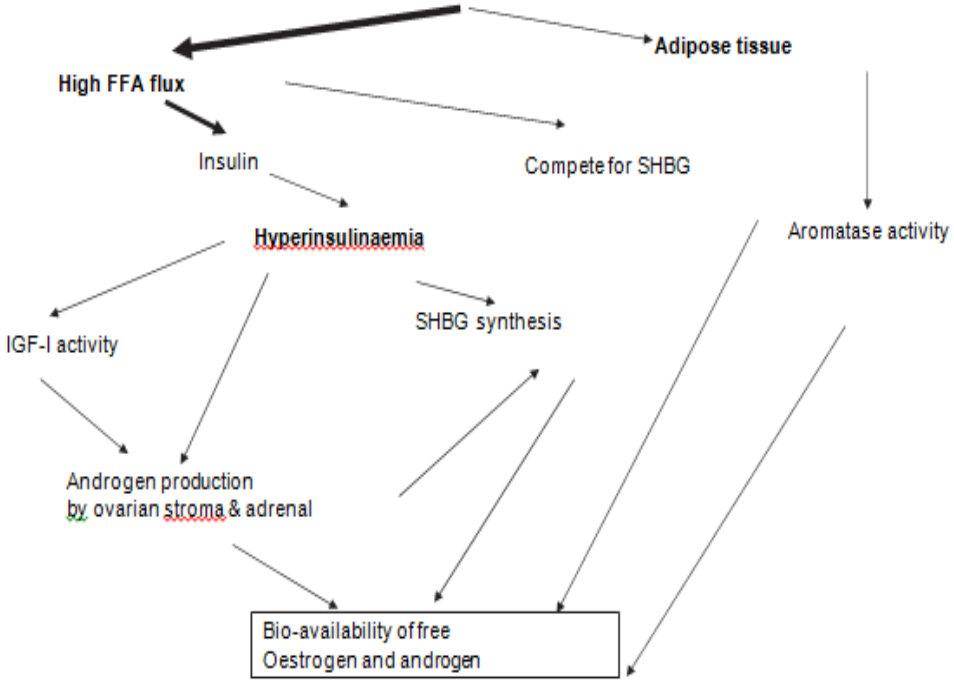


Fig: 5

Hormones:

The breast cancer survivors, who are obese, have higher bio available concentrations of tumour promoting hormones such as estrogen and testosterone, which may contribute to poor survival. Obese women have 35% higher concentrations of estrogen and 130% higher concentrations of estradiol and increased Testosterone concentrations compared with nonobese woman. Obesity is strongly and inversely associated with sex-hormone-binding globulin (SHBG)levels,suggestingthatcentralobesitywithassociated lowplasmalevelofSHBGspromotesbioavailabilityofandro- gens and estrogen.

Obese women may have hyperinsulinemia that promote mammary carcinogenesisbyincreasingthelevelsofinsulin-likegrowthfactor. (IGF), free fatty acid and leptin which have a synergistic effect to estrogen on mammary epithelial cells by promoting angiogenesis and transcriptionalfactors.Leptin, a type of adipocytokines that are produced by adipocytes have been associated with carcinogenesis, tumour migration and invasion, enhancement of angiogenesis and increased aromatase activity.

Nutrition:

The association between breast cancer risk and dietary factors has long been recognised but the complex relationship between obesity, nutrition and breast cancer is not fully understood. The regular physical activity after a breast cancer diagnosis has a strong evidence toreducethe risk of death from this disease but there is little direct evidence to show that lack ofphysical exercise leads to the development or poor prognosis of breast cancer.

TUMOUR SIZE:

Tumour size is one of the strongest prognostic indicators. When tumours are detected at their early stage we can perform a breast conserving surgery. When tumour size are larger it implies more number of tumour doubling time and the chance of distance metastatis is also high.A larger tumour has been related to more positive lymph nodes , thus their interaction further influences the survival . Tumour size plays an important role in deciding neo adjuvant chemotherapy. In this study the mean tumour size in premenopausal women and post menopausal women and their relation with BMI are studied.

AXILLARY LYMPH NODE:

Axillary lymph node status is one of the most important prognostic factors for breast carcinoma and a valuable indicator of long-term survival. Node- positive patients have about a 4–8 times higher mortality than those without nodal involvement. The more nodes involved the worse the prognosis.

Lymphnode clearance in mastectomy surgery depends on the positivity of node. Practice has changed from full dissection and/or radiation of the axilla to the use of sentinel node biopsy (SNB) for many patients. There is still debate about what constitutes an adequate axillary dissection in terms of the total number of lymph nodes removed. It is generally accepted that greater than 10 LNs are required .One study found that at least five and 10 nodes are required for node-negative and node-positive patients respectively. The LN ratio (LNR), defined as the number of positive LNs over the number of LNs removed. LNR places an important prognostic ratio.

RECEPTOR STATUS:

The breast cancer is a heterogeneous disease with variable biological and clinical characteristics because of its different genetic make-up. It is well known that Proto-oncogenes and tumor suppressor genes are two classes of genes that play a central role in the regulation of cell growth and differentiation. So any alterations in one or more of these genes appear to play an important role in the pathogenesis of most human malignancies.

ESTROGEN RECEPTOR:

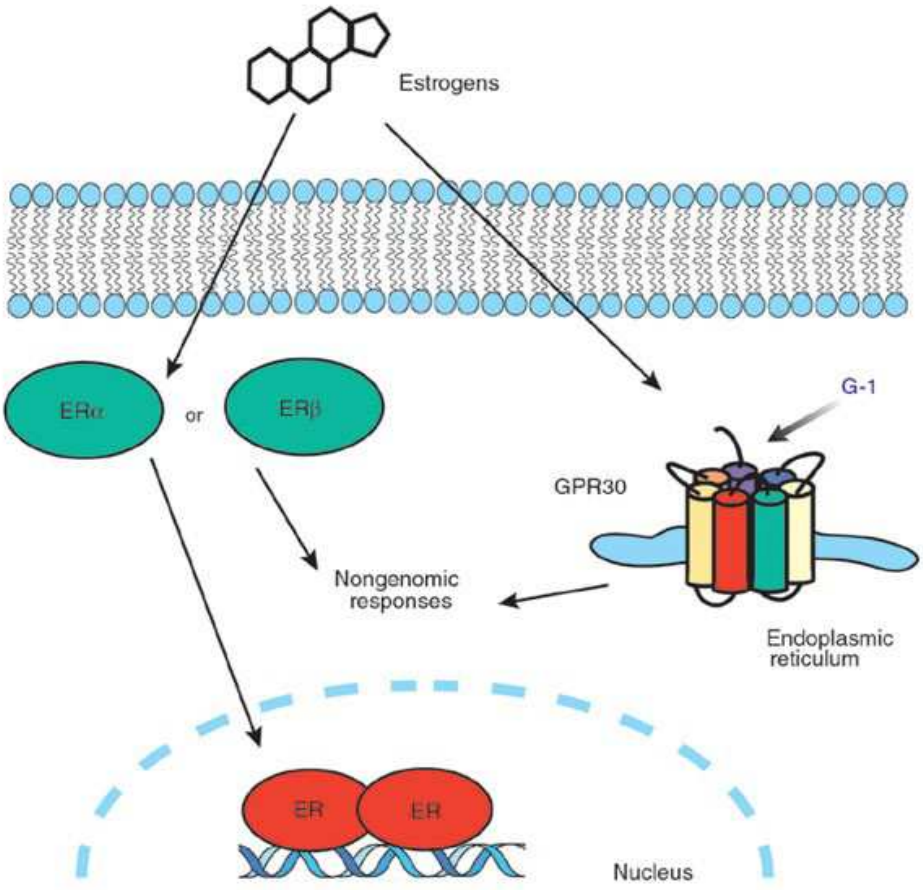


Fig: 6

Estrogen receptors (ERs) are a group of proteins found inside cells. They are activated by the hormone estrogen (17β-estradiol).Two types (G protein-coupled receptors)

- 1.ERα
- 2.ERβ

MECHANISM OF ACTION:

ER receptors, once activated by estrogen translocate into nucleus and binds to the DNA. This regulates the activity of different genes.

Distribution:

The ERα are found in

- Breast cancer cells
- Endometrium
- Ovarian stromal cells
- Hypothalamus.
- Efferent duct epithelium (males).

The ERβ are found in

- ovarian granulosa cells
- heart
- lungs
- prostate
- intestinal mucosa, endothelial cells
- Kidney, brain and bone.

The affinity differs with different ligands for binding to alpha and beta isoforms of the estrogen receptor. The agonistic and antagonistic effects of Selective estrogen receptor modulators (SERMs) at selective sites are mainly due to selective binding to either alpha or beta subtype of the receptor.

The ratio of α- to β concentration is important in certain diseases.Tamoxifen is an antagonist in breast but an ER agonist in bone and is, therefore, used as a breast cancer treatment and also prevent osteoporosis. But it increases the risk of endometrial cancer due to its partial agonistic action atendometrium.In around 70% of breast cancer cases, estrogen receptors are over- expressed and they are referred to as "ER-positive".

ER POSITIVE → TUMOUROGENESIS

TwoHypotheses has been described:

1. When estrogen binds to ER receptors, the proliferation of mammary cells get stimulated leading to increase in cell division and DNA replication. This leads to mutation.

2. Estrogen metabolism produces genotoxic waste leading to mutation.

Both these processes leads to Disruption of the cell cycle, apoptosis and DNA repair →Tumor formation

Other cancers associated with estrogen and its receptor is

- ovarian cancer
- endometrial cancer
- colon cancer
- Prostate cancer.

The concept of SERMs is based on the ability to initiate the interactions of estrogen receptors with the proteins such as

- transcriptionalcoactivators
- Transcriptionalcorepressors.

Different tissues has different ratio of coactivator to corepressor protein. Thus the same ligand may be

- agonist where the coactivatorspredominate
- antagonistic where the corepressors predominate

PROGESTERONE RECEPTOR:

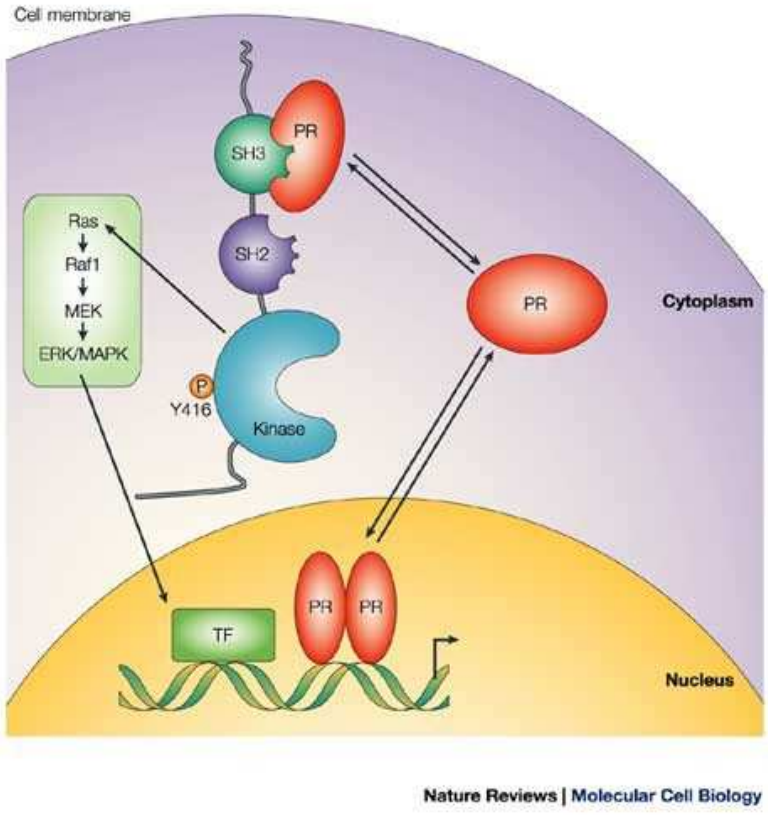


Fig: 7

The **progesterone receptor** (**PR**) also known as **NR3C3** is a protein found inside cells. It is activated by the steroid hormone progesterone.In humans, PR is encoded by a single PGR gene residing on chromosome 11q22. Three forms

- PR-A
- PR-B,
- PR-C.

The PR-B - positive regulator

PR-A and PR-C - antagonize the effects of PR-B

- No binding hormone in receptor → the carboxyl terminal of the receptor inhibits transcription.
- Binding in receptor hormone → structural change in the receptor → removes the inhibitory action of the carboxyl terminal.
- Progesterone antagonists prevent the structural reconfiguration of the receptor.

After progesterone interacts with its receptor, dimerization occurs and the Pg- PgR complex enters into the nucleus and then binds to DNA.It leads to transcription and then formation of mRNA that is translated by the ribosomes to produceproteins.

Her 2 neu (erbb2) receptors:

HER-2/neu proto-oncogene (also called c-erbB2) is located on chromosome 17q11, which encodes for p185 a transmembrane glycoprotein with tyrosinekinase activity that belongs to the family of epidermal growth factor receptors.

HER2 can dimers with their receptors leading to phosphorylation of the tyrosine residues and initiates a variety of signaling pathways. It promotes cell proliferation and also opposes apoptosis.

HER-2/neu proto-oncogene amplification or over expression is one of the most important alterations encountered in breast cancer. The amplification or over expression of HER-2/neu may lead to following:

- Largetumor size
- high grade
- lack of steroid receptor expression
- axillary lymph nodes metastasis
- advanced stage,early relapse
- Reduced overall survival.

  Increased recurrence rateHER2/neu proto-oncogene is amplified and or over expressed in approximately in 25-30% of invasive primary breast cancers .An association have become important because only patients with tumors that over express HER-2/neu benefit from antibody-based therapy with trastuzumab. For that reason, the determination of HER-2/neustatus in breast cancer is becoming more important

.

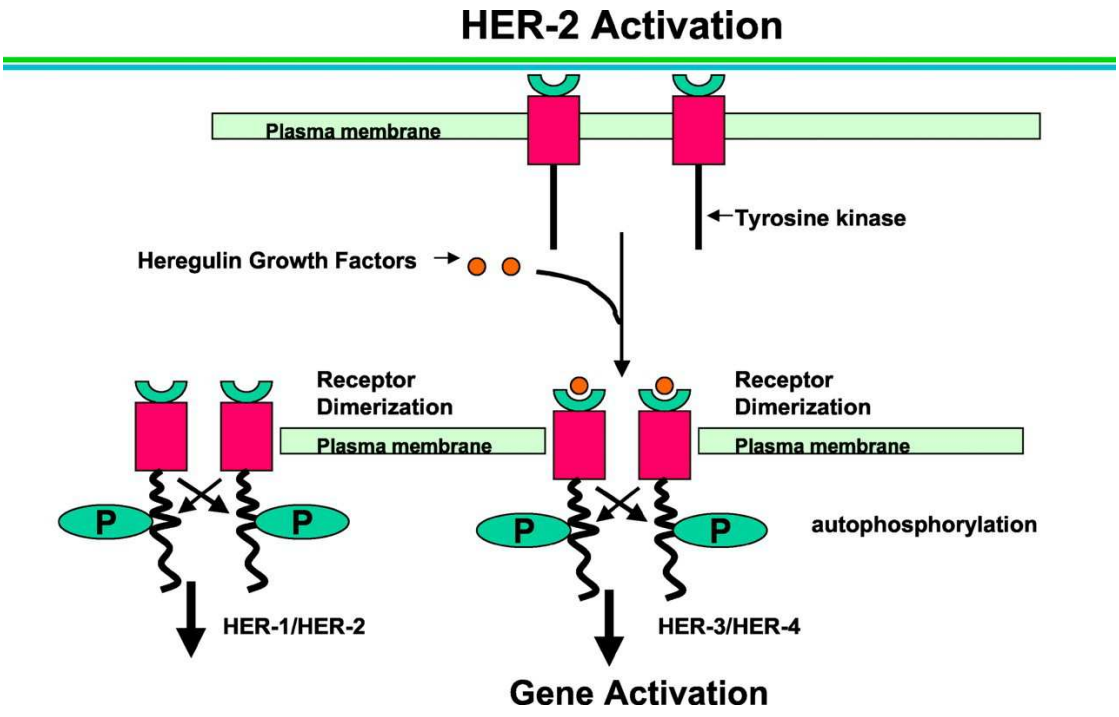


Fig: 7

The estrogen, progesterone and the Her2 neu receptors are estimated from the tissue sample using immunohistochemistry technique. Hormone receptors were considered negative whenconcentration was below 10%. P53 was consideredpositive when nuclear staining was positive in morethan 10% of tumoral cells. HER-2/neu overexpressionwas considered positive when complete and intensemembrane staining was observed in more than 10%of tumor cells.

LYMPHOVASCULAR INVASION:

Lymphovascular invasion (LVI) is defined as tumor emboli present within a definite endothelial-lined space in the breast surrounding invasive carcinoma. The existence of LVI may help identify who is at increased risk for axillary lymph node and metastasis.Lymphovascular invasion (LVI) is currently considered as an important prognostic factor for primary breast cancer. Previously it was reported that LVI is an independent prognostic factor for disease-free survival (DFS) and overall survival (OS) of patients with breast cancer.

Moreover, LVI was associated with the development of lymph node metastases and lymphatic micro vessel density. Another clinical study conducted by Krishnamurti et al showed that LVI may be associated with peripheral tumor-infiltrating lymphocytes, which have a clinical significance in breast cancer. A recent study by showed that breast cancer subtypes could affect the outcomes relatedto LVI. The prognosis of hormone receptor-negative breast cancers, such as TNBC, is suggested to be highly influenced by LVI compared to that of hormone receptor-positive breast cancers.

INVESTIGATIONS:

NONINVASIVE TESTS

MAMMOGRAPHY:

Conventional mammography delivers a radiation dose of 0.1 cGy per study.

By comparison, chest radiography delivers 25% of this dose.

However, there is no increased breast cancer risk associated with the radiation dose delivered with screening mammography.

Two types

- Screening.
- Diagnostic.

SCREENING MAMMOGRAPHY:

- Screening mammography is used to detect unexpected breast cancer in asymptomatic women
- It supplements history taking and physical examination.
- For screening mammography two views of the breast are performed.
    - ❖ Medio lateral oblique (MLO).
    - ❖ Craniocaudal

      (CC)
- The MLO view images the greatest volume of breast tissue, including the upper outer quadrant and the axillary tail of Spence.
- The CC view provides better visualization of the medial aspect of the breast and permits greater breast compression.

- But because of lower specificity of single view screening most radiologists believe that screening examination should include both MLO and CC views.

DIAGNOSTIC MAMMOGRAPHY:

- Diagnostic mammography is used to evaluate women with abnormal findings such as a breast mass or nipple discharge.
- Four views:
    - ❖ Medio lateral oblique (MLO).
    - ❖ Craniocaudal (CC).
    - ❖ 90-degree lateral
    - ❖ spot compression
- The 90-degree lateral view is used along with the CC view to triangulate the exact location of an abnormality.
- Spot compression may be done in any projection by using a small compression device, which is placed directly over a mammographic abnormality that is obscured by overlying tissues. Breast compression is a must in mammography because
    - ❖ Holds breaststill.
    - ❖ Brings objects closer tofilm.
    - ❖ Separates overlapping tissue that might obscure underlyinglesions.
    - ❖ Decreases radiation dose ofmammography.

Disadvantages of mammography:

- Pain
- Uncomfortable due to compression of breast

NORMAL FINDINGS:

- Breast entirely fat.
- Scattered fibro glandular densities.
- Breast tissue is hetero genetically dense.
- Extremely dense.

ABNORMAL FINDINGS:

- Micro stippled calcifications
- Dense stellate soft tissue mass with irregular margin and spicky projection
- Bilateral asymmetrical distribution of fibro glandular tissue.
- Architectural distortion
- Increased thickness of skin due to lymphedema
- Nipple retraction.
- Axillary LN enlargement.

DIGITAL MAMMOGRAPHY:

This type records the radiography image electronically in a digital format rather than a film. It is left in computer and is displayed on fluorescentmonitor.

ULTRASOUND:

- It is useful in evaluation of dense breast
- For screening or diagnostic in women less than 40 years
- To differentiate b/w cystic and solid masses. Unfortunately

Masses that are smaller than 5 to 10 mm may not be visualized.

MRI:

- No radiation exposure
- To differentiate scar from recurrence
- Breast with implants
- Screening of high risk woman in younger age
- Very small lesion can be determined
- Choice of imaging in pregnant female

INVASIVE TESTS:

ASPIRATION CYTOLOGY:

It uses fine needle with a syringe to aspirate cells from a suspicious area → smearing them on a glass slide → fixing them immediately (to prevent air drying) → staging for cytology.

22-23gauge needle attached to syringe is used. The air dried preparation slide is stained with wrights /wrights Giemsa / May Grunnwald Giemsa. If not air-dried it is immediately fixed with 95% alcohol and staining is done with H & E stain / with pap stain.

Combination of physical examination, mammography and FNAC will produce a diagnostic accuracy approaching 100%.FNAC is done in palpable mass, mass on mammogram. Sensitivity of test is approximately 80%; false negative varies b/w 2-10 %.

COMPLICATIONS OF FNAC:

- Growing out of tumor along needle tract, which is less in case of caliber<20 gauze.
- Acutemastitis.
- Pneumothorax.
- Haematomas.
- Interval of 2 weeks required between FNAC and mammography as they form hematomas and result in false positive mammographic studies.

CORE NEEDLE BIOPSY:

- Standard of care for biopsy of breast lesion
- 11G core needle isused.
- More invasive – more number of wedge of tissues are taken
- Able to differentiate invasive and in situ lesions
- Receptor status are assessed
- Lymphovascular lesion and grade of tumour are also assessed
- Betteraccuracy

OPEN BIOPSY:

Excision:

- When lump is less than 4 cm
- Removal of whole lump with 1 cm of clearance.

Incisional:

- When core biopsy is inconclusive
- Incision should be within the boundary of mastectomy scar
- No diathermy should be used

Galactography:

Injection of contrast into one of the ducts through the orifice of the areola. It may demonstrate ductal ectasia, obstruction / fillingdefect.

TREATMENT OF CARCINOMA BREAST:

For treatment purpose carcinoma breast is divided into 3

- Early breast cancer
- Locally advanced carcinoma breast
- Metastatic breast carcinoma

EARLY CARCINOMA BREAST

Includes -

T1N0, T2NO, T1N1, T2N1, T3NO

The main mode of treatment in early breast carcinoma is breast conservative surgery. It includes

BREAST CONSERVATIVE SURGERY:

- wide local excision of tumour
- axillary sampling
- post op radiotheraphy
- Regular follow up.

The breast specimen that is removed is oriented before sent for pathology. This allows focal reexcision of involved margins rather than global reexcision and thus improves the cosmetic result. The surgical defect created after lumpectomy is closed in cosmetic fashion by using advancement flap closure method.

Surgical staging of the axilla is performed through a separate incision in most patients undergoing breast conservation. Anatomic axillary node dissection in replaced by selective lymph nodal excision in clinically negative axillary nodes.

FACTORS INFLUENCING BREAST CONSERVATION SURGERY:

Tumor Size.

Lumpectomy is considered regardless of size of tumour, if can be excised with clear margins and an acceptable cosmetic result.

Tumors 5 cm in size, clinically positive nodes and tumors with lobular and ductal histology were included in therandomized trials of mastectomy versus breast-conserving therapy

Margins:

The positive margins were associated with a twofold increase in ipsilateral breast tumor recurrence risk compared with negativemargins. The clinicopathologic features, biology, endocrine therapy, administration of radiotherapy have no significant effect

Histology

Invasive lobular cancers and cancers with an extensive intraductal component can be treated with lumpectomy if clear margins canbe achieved. Atypical hyperplasia (ductal and lobular) and LCISat resection margins do not increase local recurrence rates.

Patient Age

Local recurrence rates after breast-conserving surgery are higher for younger women than for older women. The use of radiation therapy reduces local recurrence in patients of all ages.

All patients undergoing breast conservation surgery should

receive radiotheraphy post operatively. Any patients who have contraindication for RT are not the candidate for breast conservation theraphy.

CONTRAINDICATION FOR RADIOTHERAPHY
Absolute • Pregnancy Relative • Systemic scleroderma* • Active systemic lupus erythematosus* • Prior radiation to breast or chest wall • Severe pulmonary disease • Severe cardiac disease (if tumor is left-sided) • Inability to lie supine • Inability to abduct arm on affected side • p53 mutation†

TABLE: 2

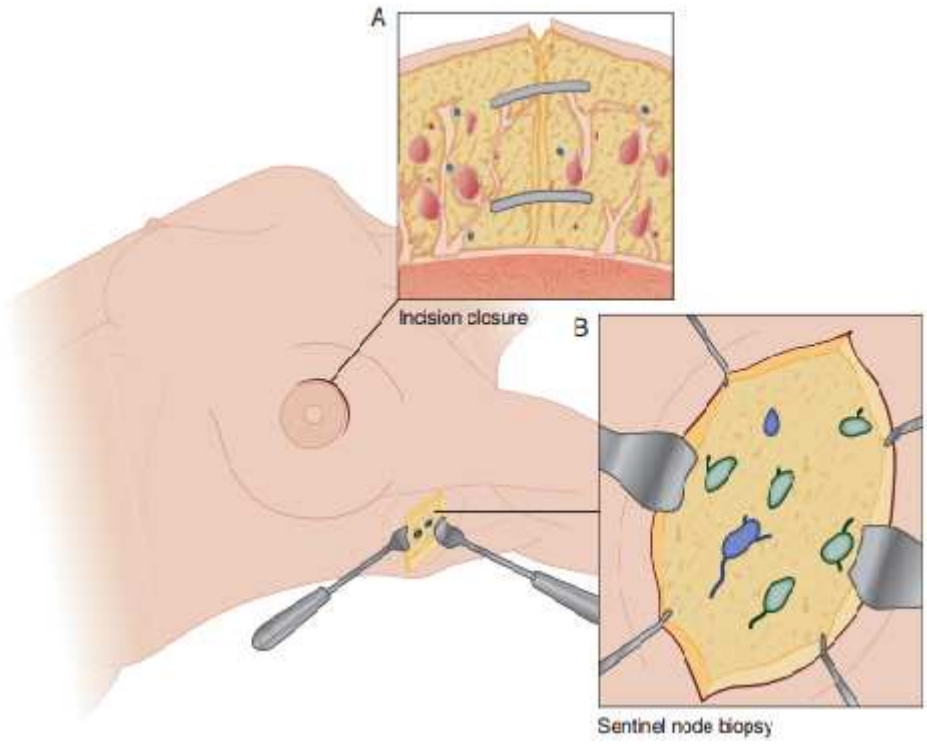


Fig: 8

Tumor that require mastectomy are following

- large tumour breast ratio
- Tumors with extensive calcifications on mammography
- tumors for which clear margins cannot be obtained on wide local excision
- tumors in patients with contraindications to breast irradiation
- Patient preference for mastectomy or a desire to avoid radiation is also a valid indication for mastectomy.

MODIFIED RADICAL MASTECTOMY:

Modified radical mastectomy refers to removal of

- The mammary gland
- nipple and areola
- Axillary lymph node dissection (level 1 and 2 sometimes level 3) (ALND).

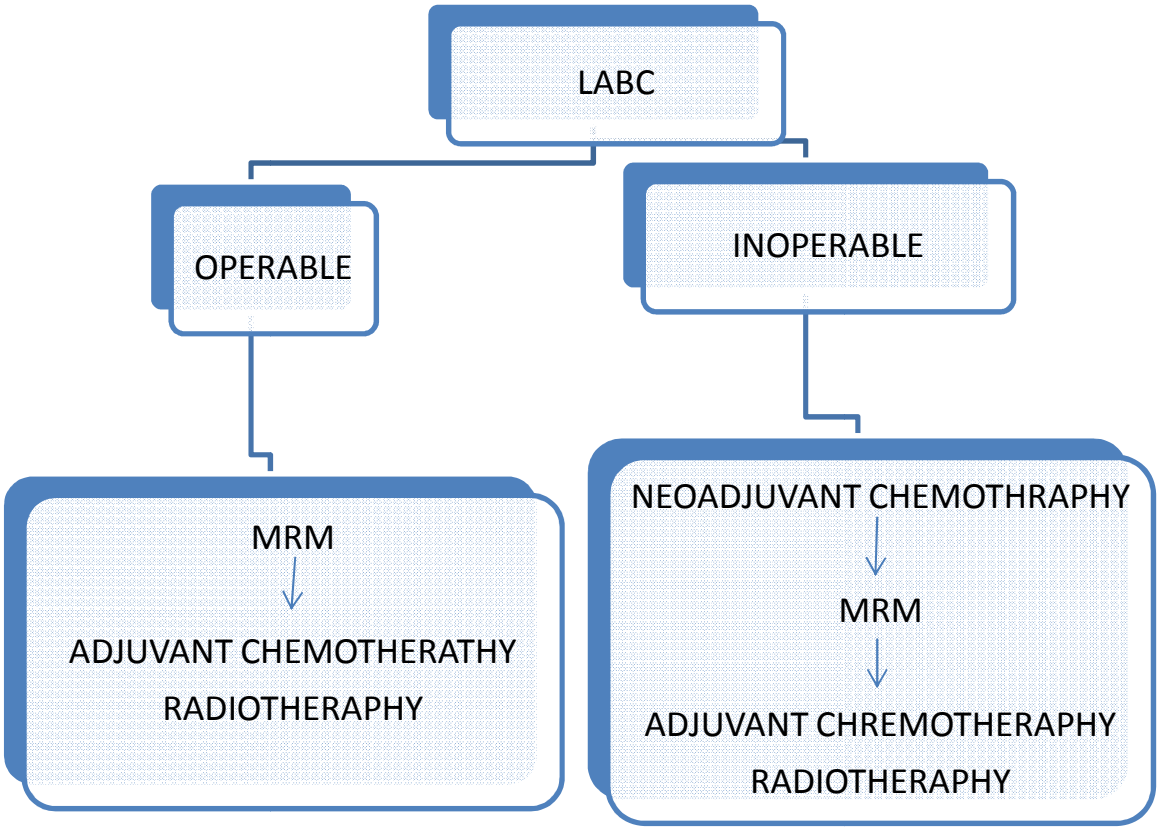
An elliptical skin incision is planned to include the nipple and areola and usually any previous excisional biopsy scars. Skin flaps are raised to separate the underlying gland from the overlying skin along the sub dermal plexus.

If immediate reconstruction is not planned, sufficient skin is taken to allow smooth closure of skin flaps without redundant skin folds; this facilitates comfortable use of breast prosthesis.

If immediate reconstruction is planned, a skin-sparing mastectomy may be performed in which only the nipple-areola complex is removed and the maximum amount of skin is left for use in the reconstruction.

Fig: 9

LOCALLY ADVANCED CARCINOMA BREAST:



METASTATIC CARCINOMA BREAST:

- Only palliative care
- Toilet mastectomy
- Palliative chemotheraphy and radiotheraphy

CHEMOTHERAPHY:

It is give as 3 forms

- Neo adjuvant
- Adjuvant
- Palliative

Despite advances in surgical treatment, most of the woman develops metastasis with in 5 to 10 years. Hence chemotherapy is a most important modality of treatment in carcinoma breast.

Most common used are anthracyclins and taxanes.

Most common regimen used is CMF regimen (cyclophosphamide, Methotrexate, 5- fluorouracil

Other regimens are CAF, AC, and CEF.

TABLE 34-8 **American Society for Radiation Oncology Guidelines for Accelerated Partial Breast Irradiation**

FACTOR	"SUITABLE" GROUP	"CAUTIONARY" GROUP	"UNSUITABLE" GROUP
Patient factors			
Age (yr)	≥60	50-59	<50
Tumor factors			
Tumor size (cm)	≤2	2.1-3.0	>3
T stage	T1	T0 or T2	T3 or T4
Margins	Negative by at least 2 mm	Close (<2 mm)	Positive
Histology	Invasive ductal carcinoma or other favorable subtypes	Invasive lobular carcinoma	NA
Pure DCIS	Not allowed	≤3 cm in size	>3 cm in size
Grade	Any	NA	NA
LVI	None	Limited/focal	Extensive
ER status	Positive	Negative	NA
Multicentricity	Unicentric	NA	If present
Multifocality	Clinically unifocal with total size ≤2 cm	Clinically unifocal with total size 2.1-3 cm	Clinically multifocal or microscopically multifocal >3 cm in total size
Nodal factors			
N stage	pN0	NA	pN1-3
Treatment factors			
Neoadjuvant chemotherapy	Not allowed	NA	If used

Table: 3

RADIATION THERAPHY:

Radiotherapy is mainly for locoregional control of disease. It is given as

- Adjuvant therapy
    - ❖ Brest conservation surgery
    - ❖ MRM
- Palliative therapy

Target volume:

AFTER BCS

- Whole breast RT
- Lumpectomy boost
- Regional nodes

AFTER MASTECTOMY

- Chest wall
- Scar
- Regional nodes

DOSE OF RADIATION

Conventional:

50 Gy in 25 daily fractions - 5 weeks

Hypo fraction:

40 Gy in 15 daily fractions 2.65 Gy - 3 weeks

BREAST BOOST RADIATION TO TUMIUR BED:

16 Gy in 8 daily fractions- 1.5 weeks

10 Gy in 5 daily fractions- 1 week

LYMPH NODE RADIATION:

50 Gy in 25 daily fractions - 5 weeks

40 Gy in 15 daily fractions - 3 weeks

PALLIATIVE DOSE:

30 Gy / 10#

8 Gy / 1#

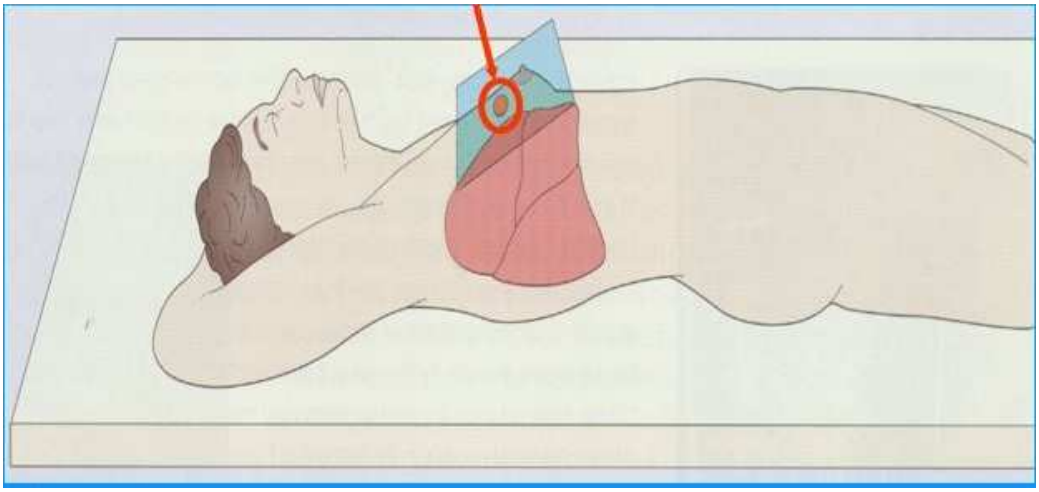


Fig 10

METHODOLOGY

METHODOLOGY:

Study Design	**Observational study (Prospective)**
Sample Size	160
Inclusion Criteria	All the carcinoma breast patients diagnosed clinically and confirmed by trucut biopsy undergoing MRM BODY MASS INDEX – 16 to 40(Normal to severely obese) BMI: 16 -25 Normal BMI: 25 – 40 Overweight and obese
Exclusion Criteria	Advanced carcinoma of breast Carcinoma breast with metastasis Undergoing neoadjuvant chemotherephy Very severely obese patients(BM >.40) Severely underweight (BMI <16)
Ethics Clearance	Applied

Investigations	All Patients who fit the inclusion criteria will be observed and following data collected • USG breast (age less than 40 years) / mammogram of other breast (age more than 40 years) • Trucut biopsy • CT Chest • Skeletal survey/ Bone scan • USG abdomen
METHODOLOGY	All patients who fulfill the inclusion criteria will be enrolled. Written informed consents will be obtained. Biopsy proven patients only will be included in the study. Trucut biopsy will be taken and samples were submitted for histopathology, determination of estrogen, progesterone receptor expression and HER-2/neu status. Associations with other characteristics like age, menopausal status, body mass index, tumour size, and node will also be studied. I will do the investigations mentioned above. Will stage the carcinoma breast based on TNM classification Based on staging will proceed with modified radical mastectomy followed by adjuvant theraphy. The resected segment will be sent for histopathology to study the lymphovascularinvolment.

SAMPLE SIZE CALCULATION:

Based on the study titled “comparison of ER, PR and HER-2/neu (c-erbB2) reactivity pattern with histologic grade, tumour size and lymph node status in breast cancer done by Azizun - Nisa, bhurgri Y, Raza F Kayani N

$$n = \frac{Z^2 pq}{d^2}$$

When Z = 1.96 for α 0.05; P= 24.7; q = 75.3 d is fixed as 7%

$$n = \frac{1.96 \times 1.96 \times 24.7 \times 75.3}{7 \times 7} = 146$$

Assuming a non response rate of 10%, sample size is fixed at 146+14=160

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. The Odds ratio and relative risk was used to find the effect of cause. In all the above statistical tools the probability value .05 is considered as significant level**.**

RESULTS

RESULTS

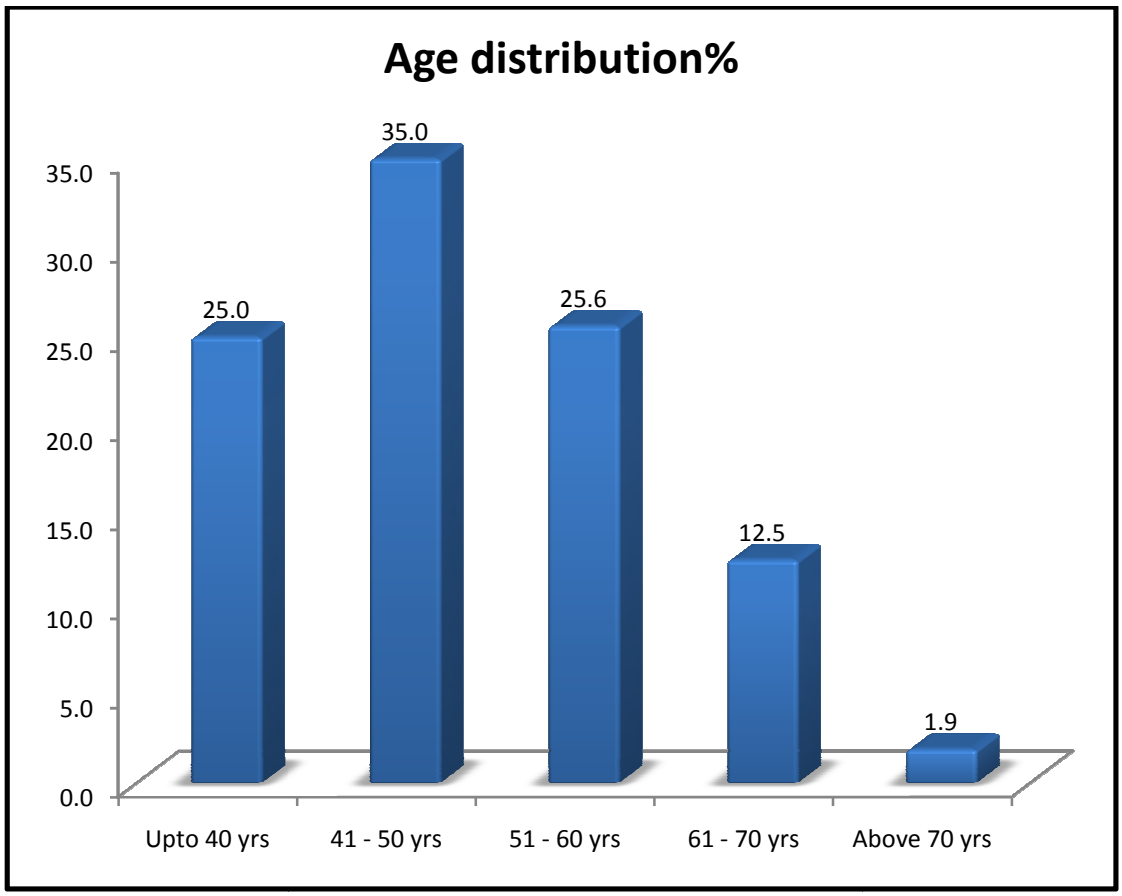
About 160 women who were affected with carcinoma breast were included in this study based on my inclusion and exclusion criteria. All women are biopsy proven carcinoma breast and underwent surgery as primary treatment.

AGE DISTRIBUTION:

Among the 160 women, 40(25%) were under 40 years, 56(35%) were between 41 to 50 years, 41(25.6%) were between 51 to 60 years, about 20 (12.5%) were between 61 to 70 years and only 3 (1.9%) were above 70 years. Thus most of the patients in my study were between 41 to 50 years.

AGE		Frequency	Percent
Valid	Up to 40 yrs.	40	25.0
	41 - 50 yrs.	56	35.0
	51 - 60 yrs.	41	25.6
	61 - 70 yrs.	20	12.5
	Above 70 yrs.	3	1.9
	Total	160	100.0

Table: 4



Graph: 1

Mean age of women getting carcinoma breast in my study is 48.57 years of age.

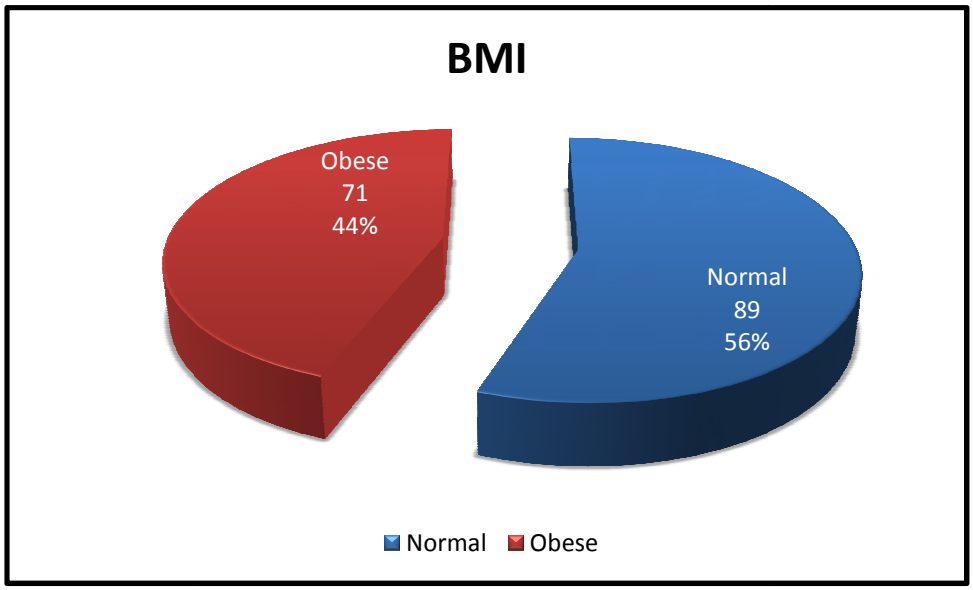
BMI:

In my study, i took the women having BMI between 16 to 25 as normal and BMI between 26 to 40 as obese. Among 160 women, 89(55.6%) were normal BMI whereas 71(44.4%) were obese.

BMI

		Frequency	Percent
Valid	Normal	89	55.6
	Obese	71	44.4
	Total	160	100.0

Table: 5

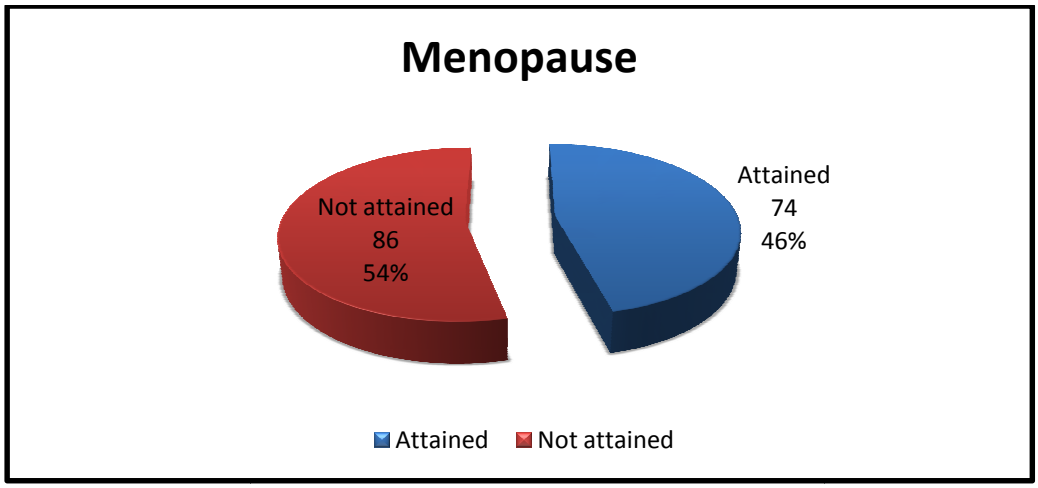


Graph: 2

In my study the mean BMI value of woman getting carcinoma breast was 25.019 years of age.

MENOPAUSAL STATUS:

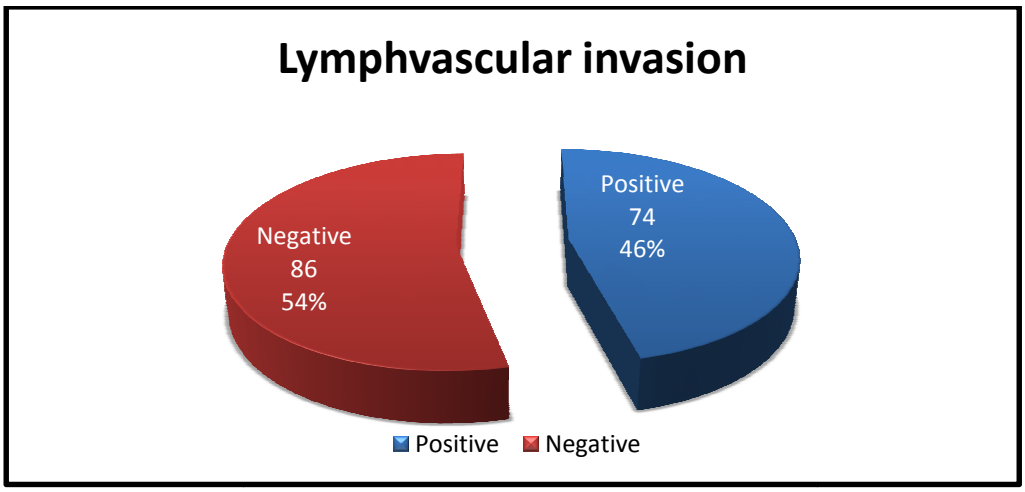
In my study, 86(54%) women had breast cancer after attaining menopausewhereas 74(46%) of women had breast cancer before attaining menopause.



Graph: 3

LYMPHOVASCULAR INVASION

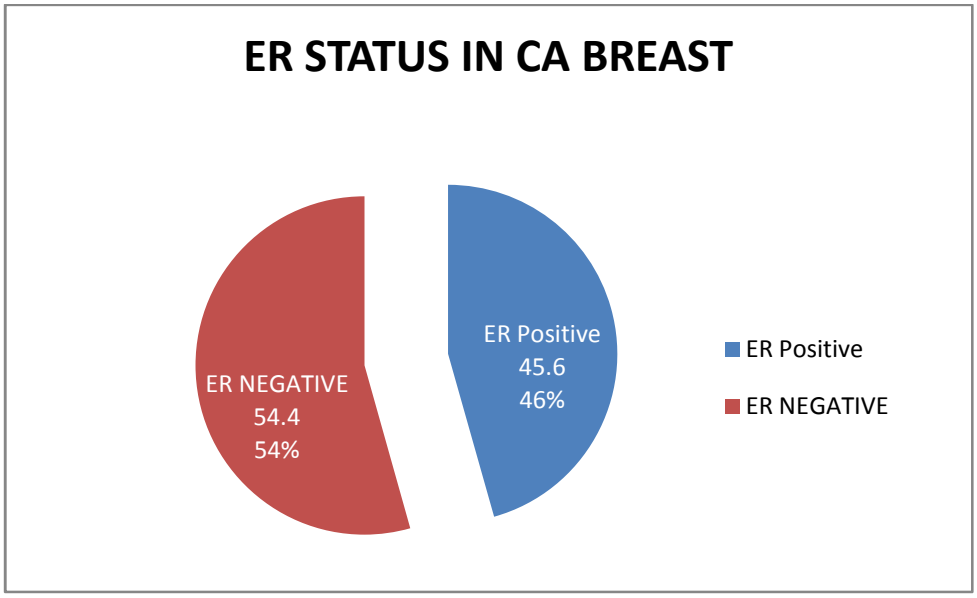
Among the 160 carcinoma patients 74(46%) patients have lymphovascular invasion where remaining 86(54%) has no lymphovascular invasion.

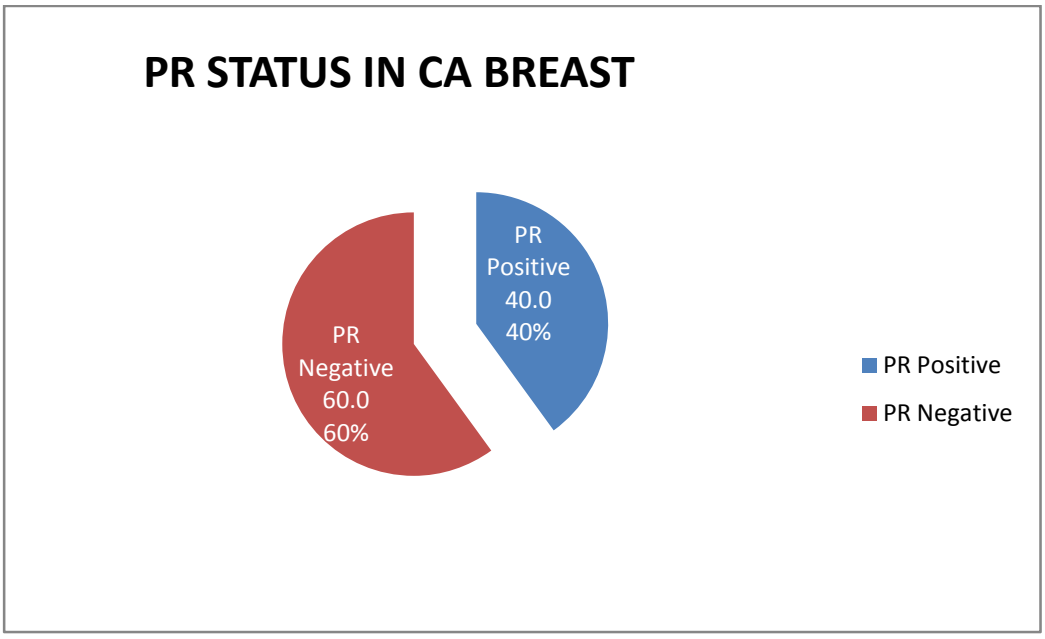


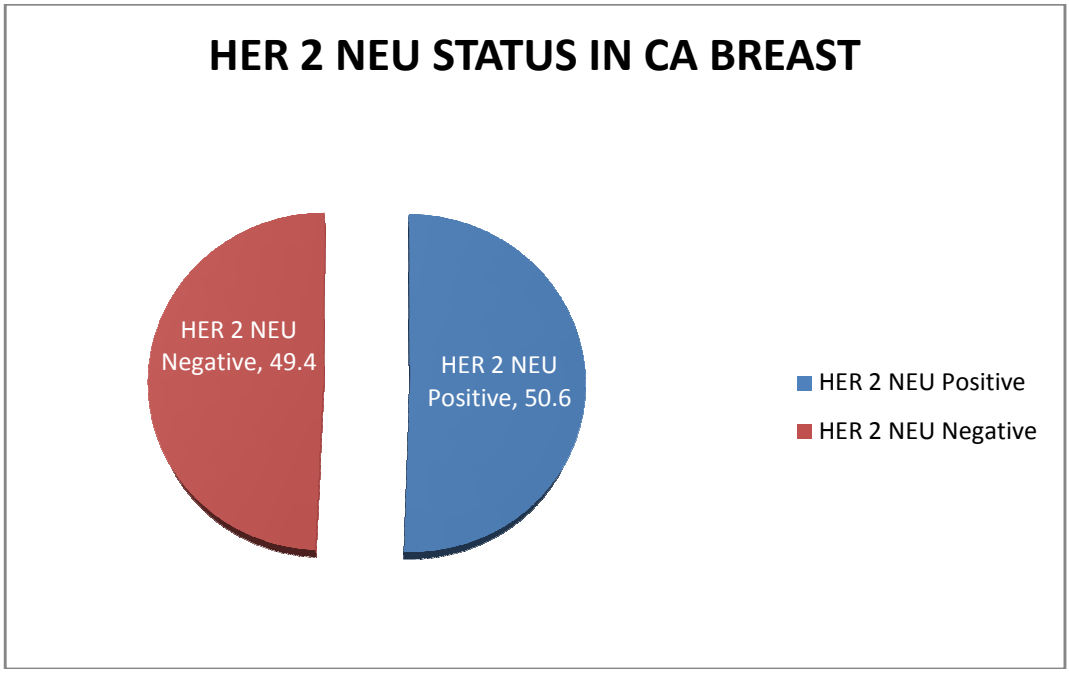
Graph: 4

ER, PR AND HER 2 NEU RECEPTOR STATUS:

In this study of 160 carcinoma breast women, 54% has ER receptor positive status, 60 % has PR receptor positive status and 49.4 % has HER 2 NEU receptor positive status. Among them 36.3% have both ER, PR receptor positive status.







Graph: 5

Descriptive Statistics

In this study the following mean values are observed

	N	Minimum	Maximum	Mean	Std. Deviation
AGE_A	160	24	76	48.74	9.812
HEIGHT	160	143	171	155.10	5.786
WEIGHT	160	40	86	60.08	9.229
BMI	160	19.0	34.4	25.019	3.6763
Valid N (list wise)	160				

Table: 6

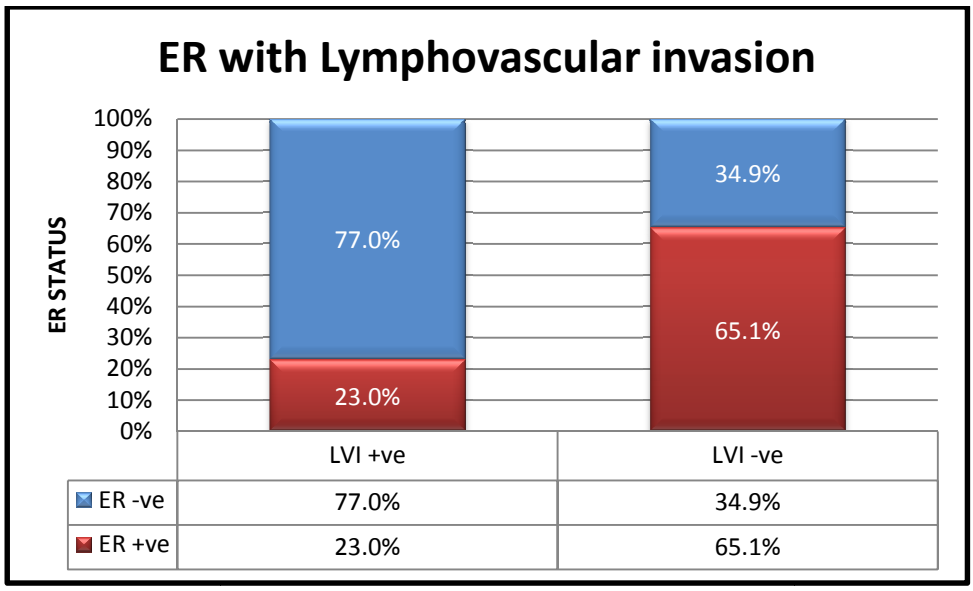
CORRELATION DATAS:

In this study on carcinoma breast the following prognostic factors were correlated and their relationship was studied.

1. Receptor status with lymphovascular invasion:

ER receptor status with lymphovascular invasion:

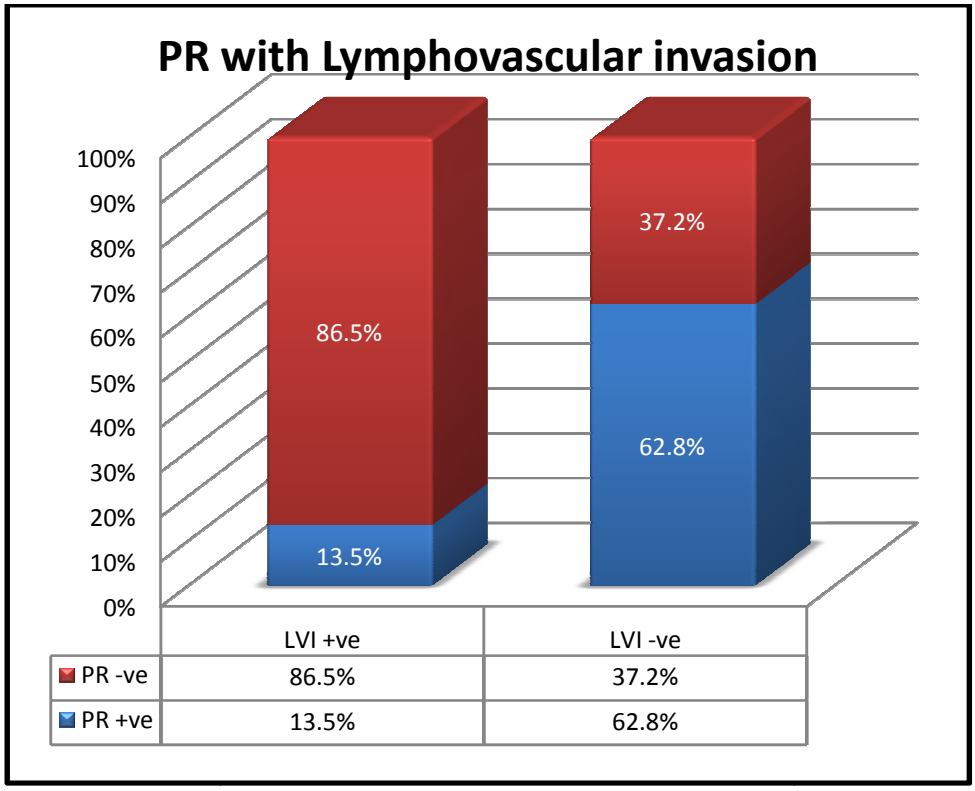
In this study among the patient with lymphovascular invasion, majority (77%) has negative ER receptor status whereas those without lymphovascular invasion majority show positive ER receptor (65.1%) status.



Graph: 6

PR RECEPTOR STATUS WITH LYMPHOVASCULAR INVASION:

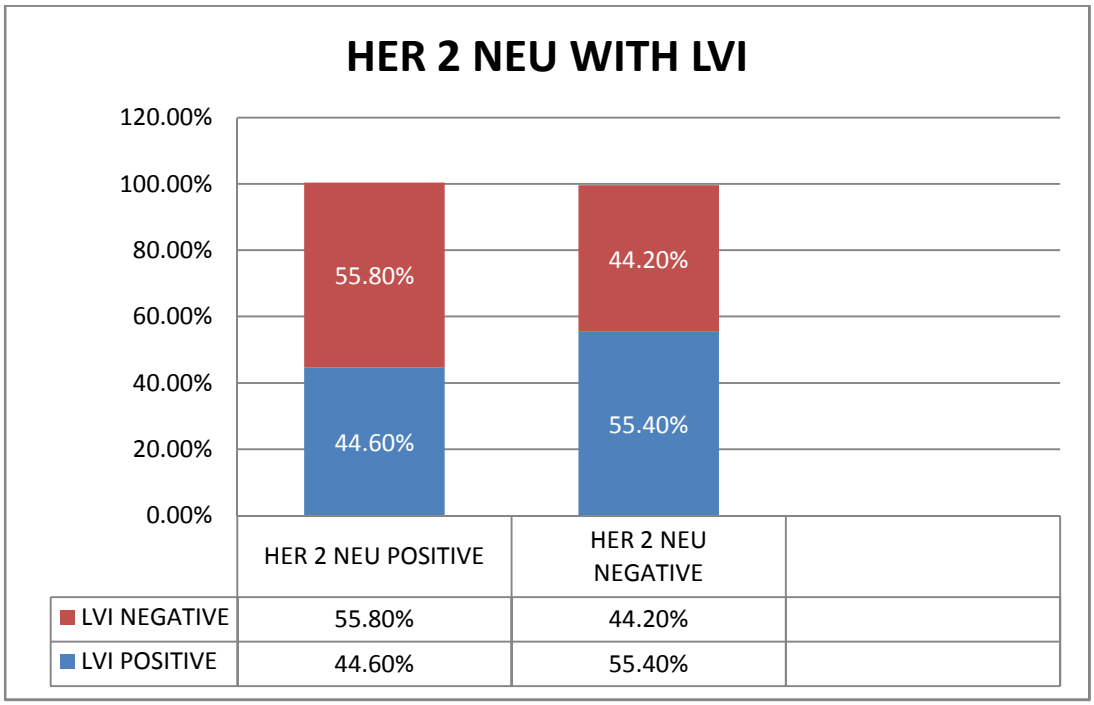
In this study among the patient with lymphovascular invasion, majority (86.5%) has negative PR receptor status whereas those without lymphovascular invasion majority show positive PR receptor (62.8%) status.



Graph: 7

HER 2 NEU RECEPTOR STATUS WITH LYMPHOVASCULAR INVASION:

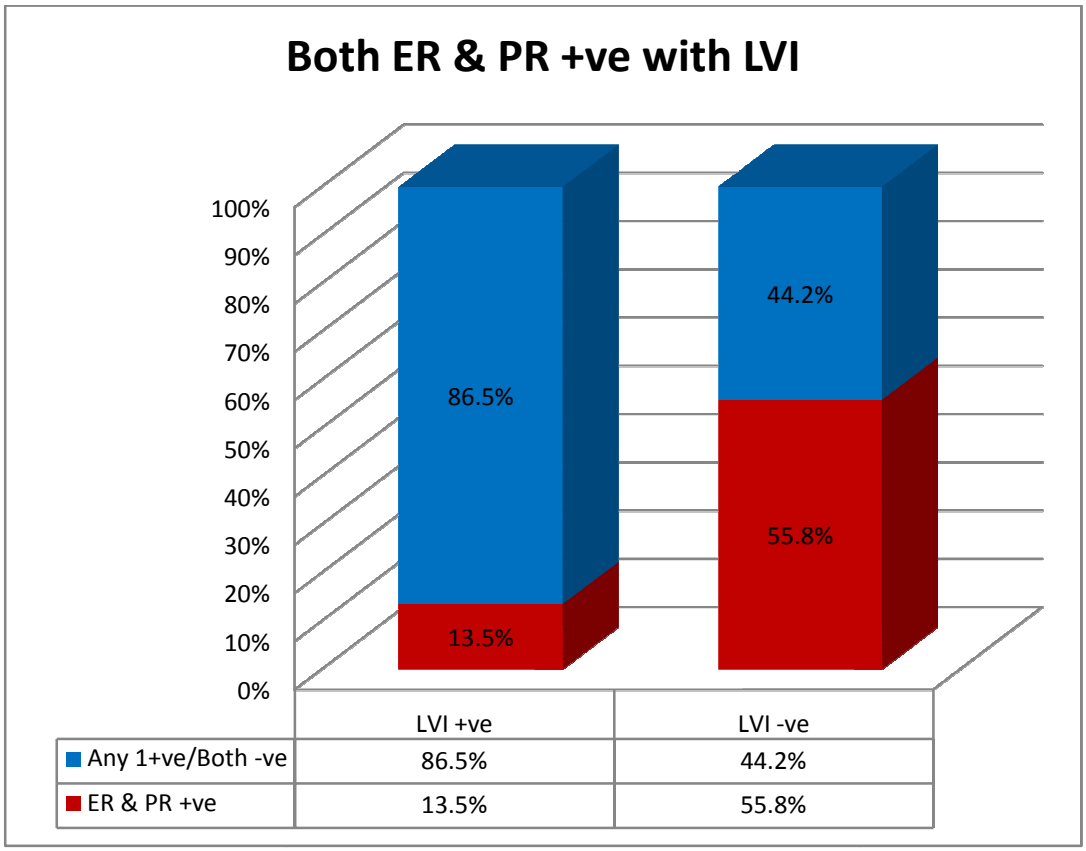
In this study among the patients having lymphovascular invasion, 44.60% has positive HER 2 NEU status whereas 55.4 % has HER 2 NEU negative status.



GRAPH: 8

BOTH ER, PR RECEPTOR STATUS WITH LYMPHOVASCULAR INVASION:

Among the patients affected with lymphovascular invasion only 13.5 % shows positive ER, PR receptor status whereas 55.8% of positive ER, PR receptors status has no lymphovascular invasion.

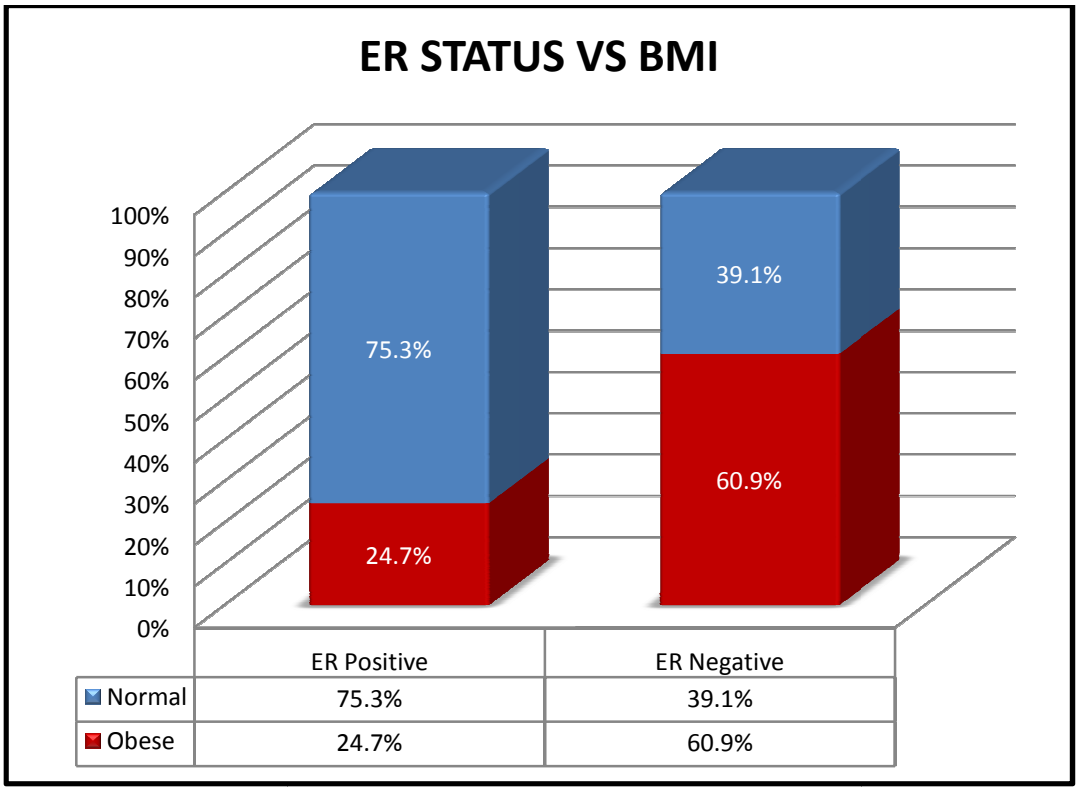


Graph: 9

2. Receptor status with BMI:

ER RECETOR STATUS VS BMI:

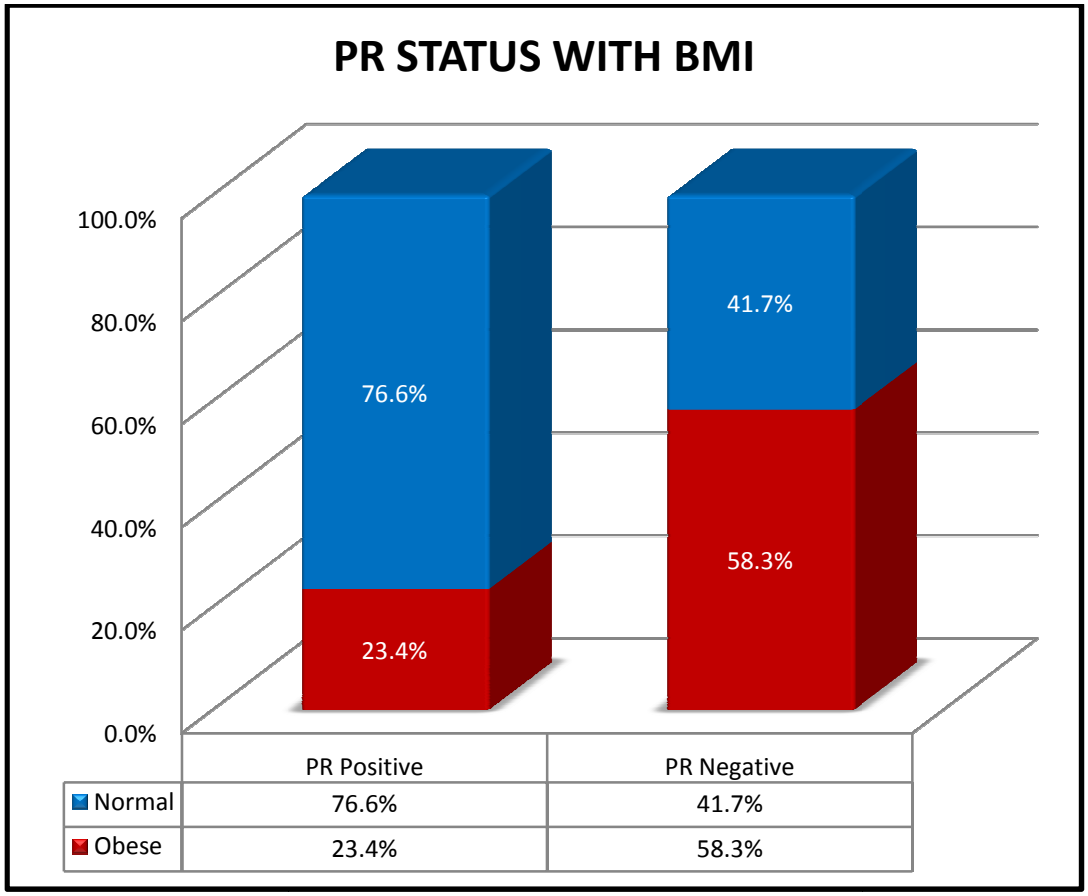
In this study 75.3 %(majority) of carcinoma breast patients with ER positive status has normal BMI whereas only 24.7 % are obese and among negative ER receptor status majority (60.9%) were obese.



Graph: 10

PR RECETOR STATUS VS BMI:

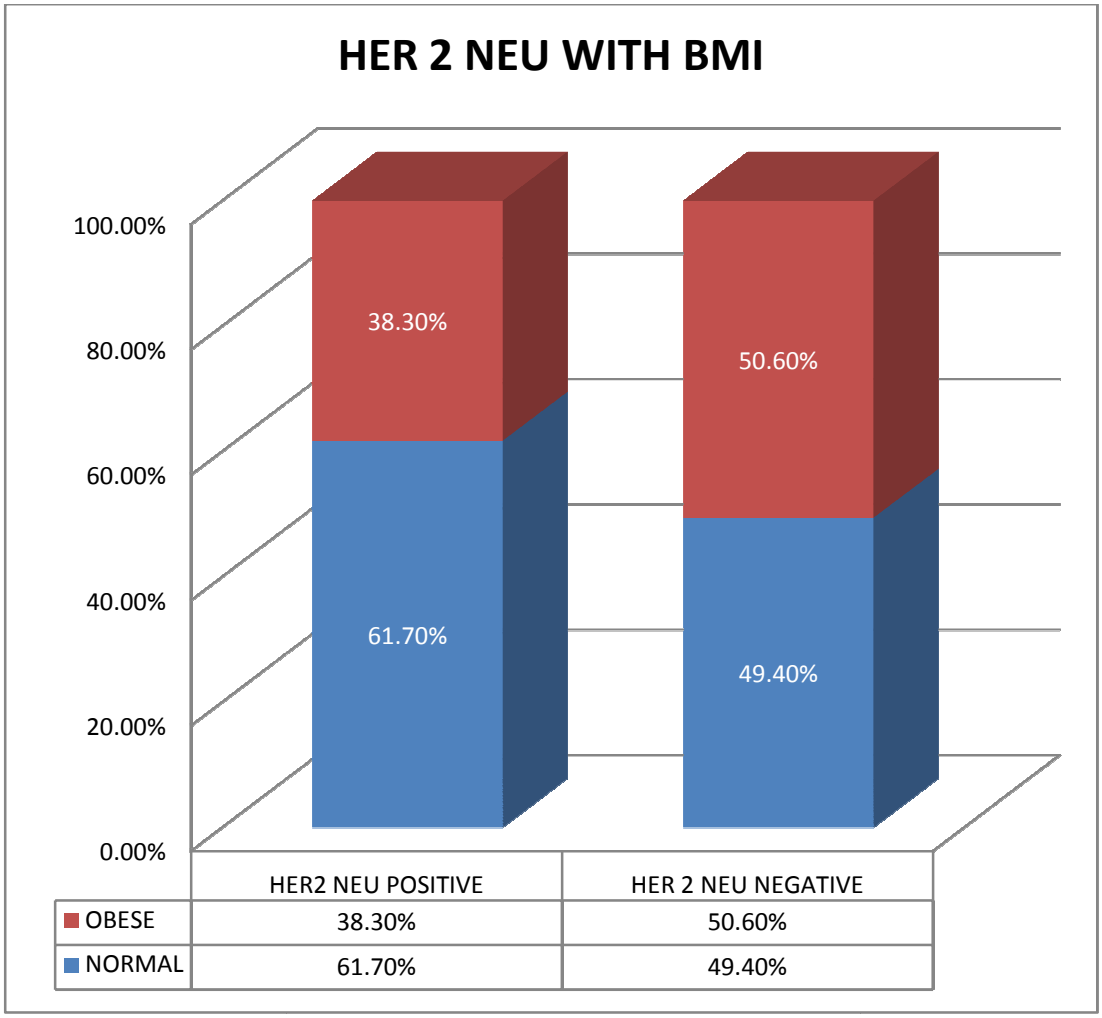
In this study 79.63 %(majority) of carcinoma breast patients with PR positive status has normal BMI whereas 23.4 % are obese, whereas among negative PR receptor status 58.3% were obese.



GRAPH: 11

HER 2 NEU RECETOR STATUS VS BMI:

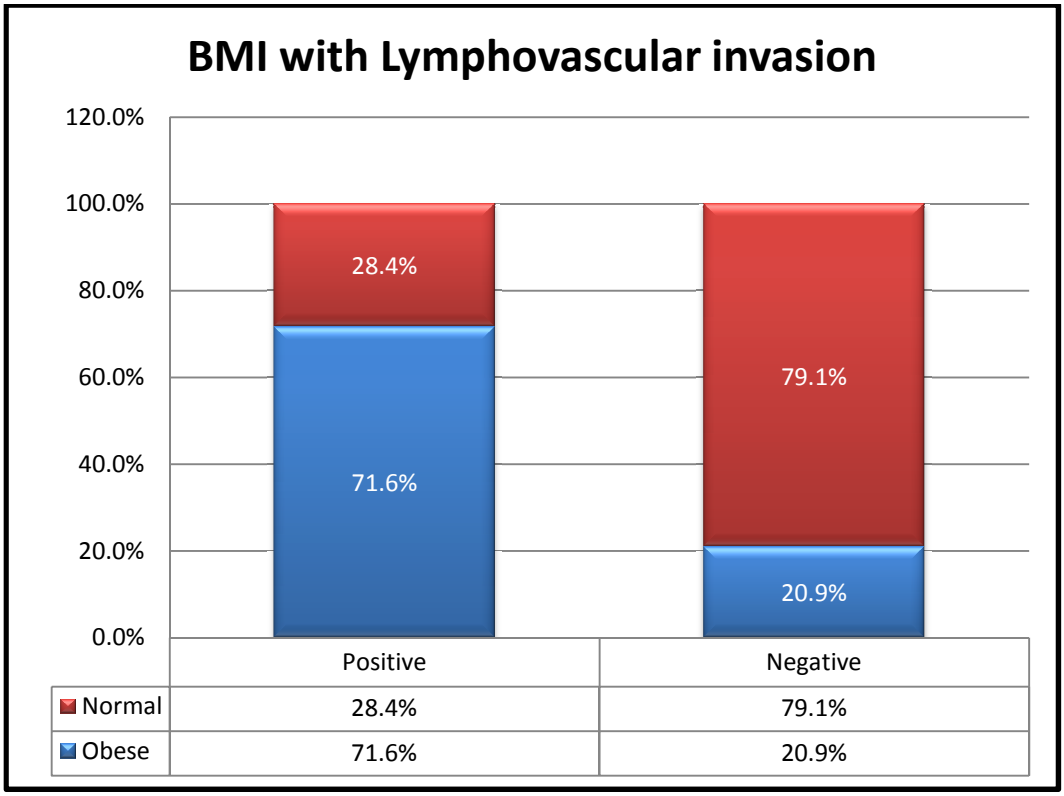
In this study among the patients having POSITIVE HER 2 NEU, 61.7 %(majority) has normal BMI whereas 38.3% are obese.



Graph: 12

BMI VS LVI:

Among the patients who has lymph vascular invasion in this study, 71.6 % (majority) are obese with BMI more than 25 whereas in those without lymph vascular invasion majority (79.1) are normal with BMI less than 25.

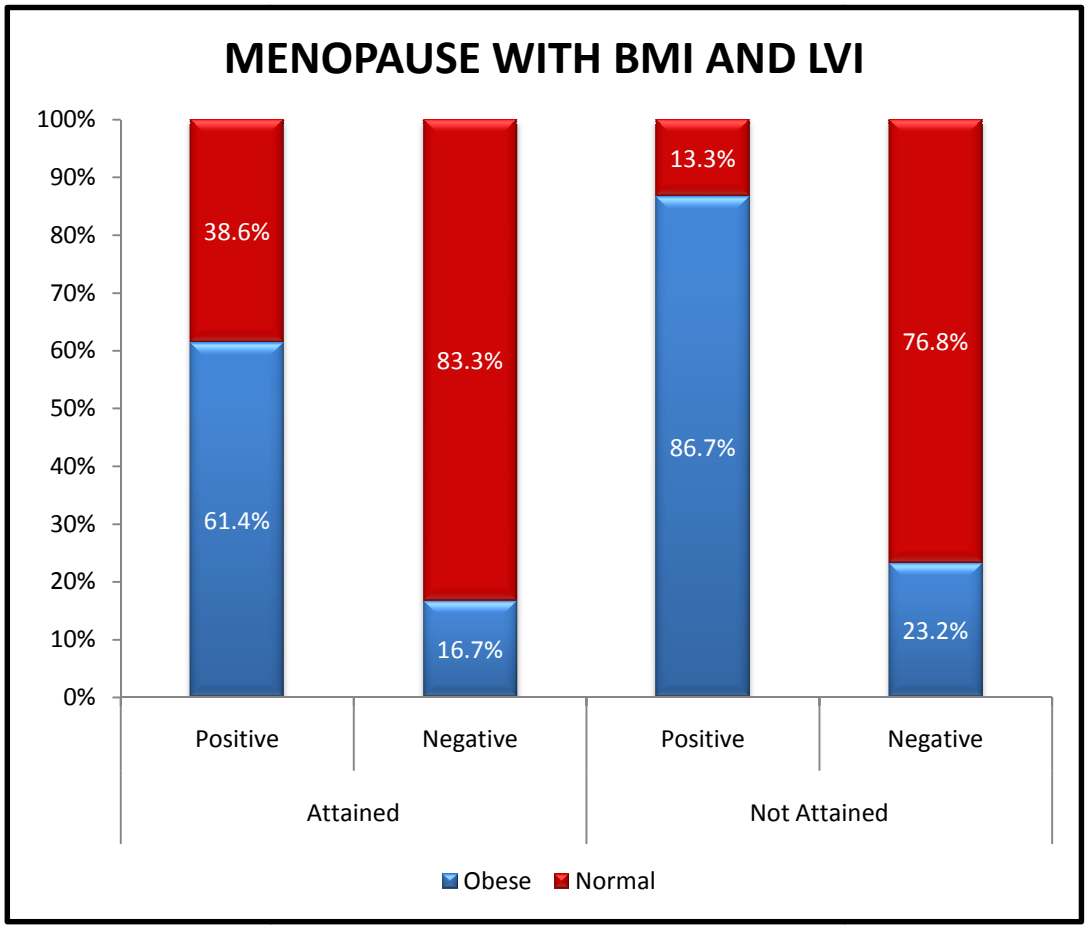


Graph: 13

BMI VS LVI VS MENOPAUSE:

Among the postmenopausal woman, positive lymphovascular invasion are noted mainly (61.4%) in women with BMI more than 25(obese). Negative lymphovascular invasion are noted mainly in normal women (83.3%) with BMI less than 25.

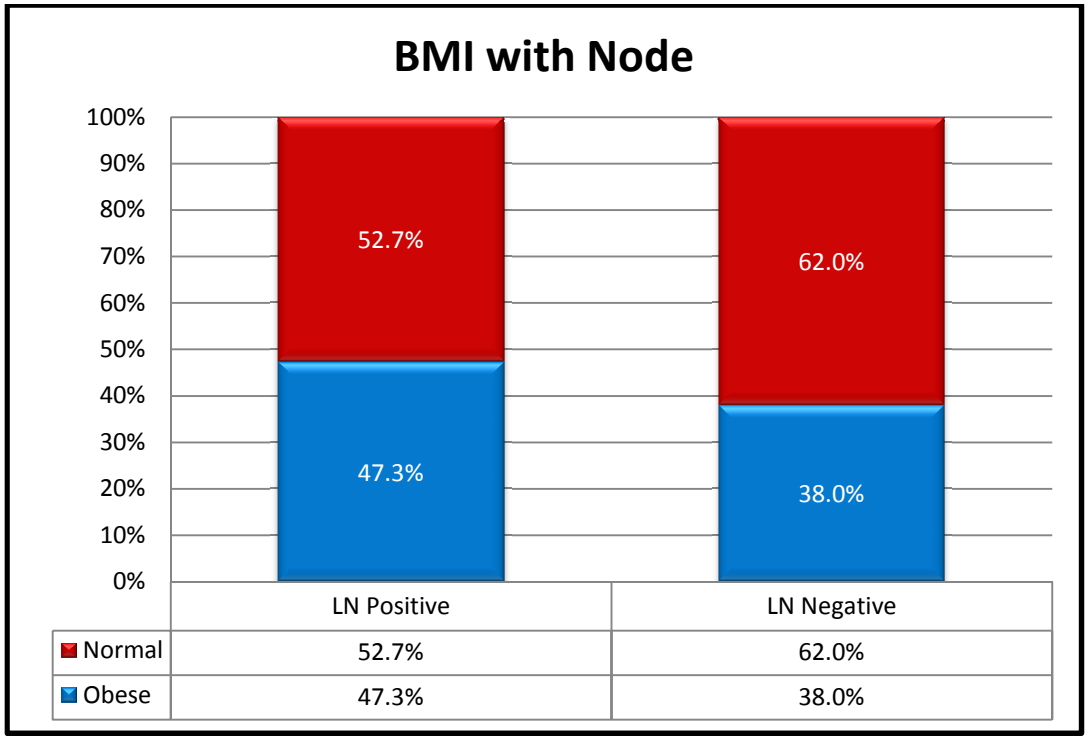
Among the premenopausal women, positive lymphovascular invasive are noted mainly in obese woman (86.5%) whereas negative lymphatic invasion are noted mainly (76.5%) in normal women.



GRAPH: 14

4. BMI VS NODE:

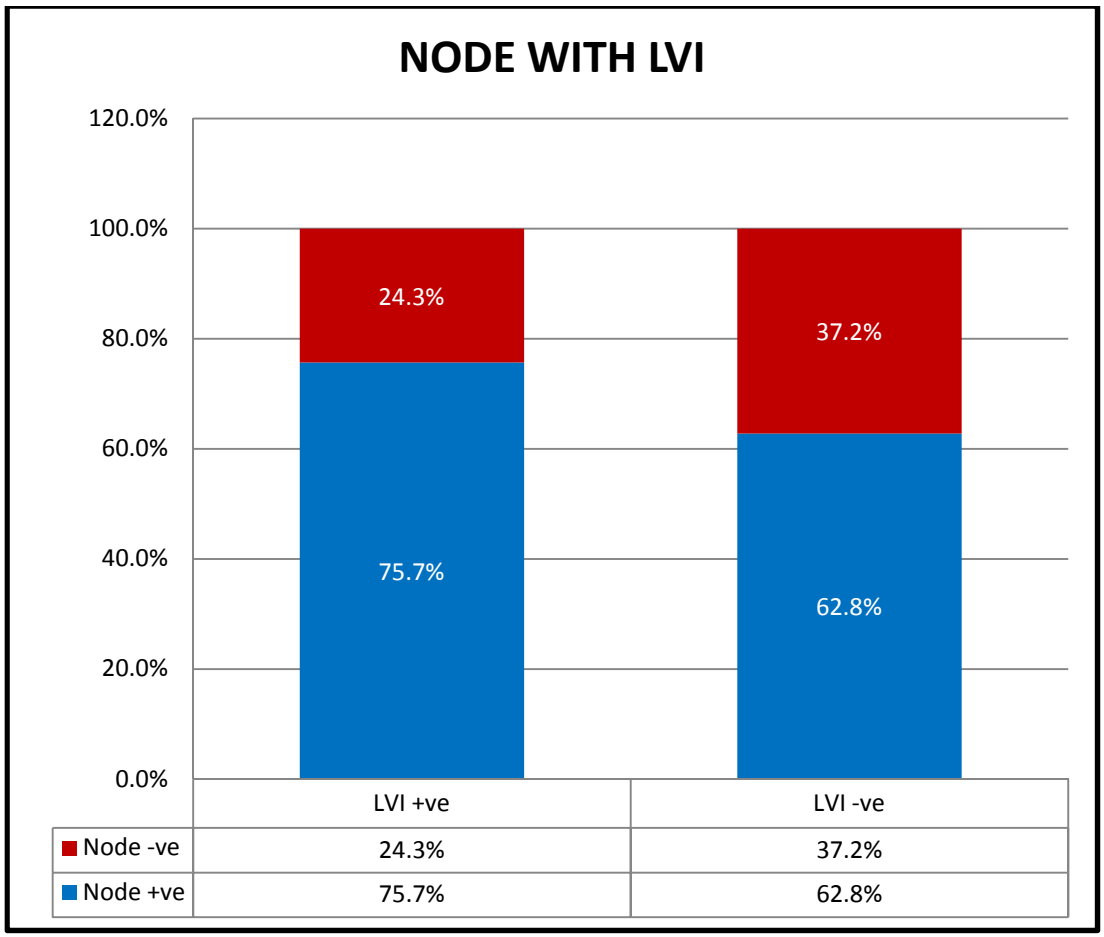
Among the node positivity tumor patients, 52% has normal BMI whereas 47.3% has high BMI (Obese). Among the node negativity 62% are normal and 38% are obese.



Graph: 15

5. NODE VS LVI:

Node positivity is noted in 75.7% of patients with lymphovascular invasion and 62.8% noted in patients without lymphovascular invasion.



Graph: 16

ODDS RATIO AND P VALUES FOR VARIOUS PROGNOSTIC FACTORS

		ODDS RATIO	P VALUE
ER STATUS	**BMI**	0.210	**0.0005**
PR STATUS	**BMI**	0.219	**0.0005**
HER 2 NEU STATUS	BMI	-	0.116
ER STATUS	**LVI**	0.160	**0.0005**
PR STATUS	**LVI**	0.093	**0.0005**
HER 2 NEU STATUS	LVI	-	0.157
BMI, PREMENOPAUSAL	**LVI**	21.5	**0.0005**
BMI, POSTMENOPAUSE	**LVI**	9.53	**0.0005**
NODE	LVI	1.844	0.08
NODE	BMI	1.463	0.274

Table: 7

DISCUSSION

DISCUSSION:

In this observation study we studied the association between various prognostic factors of carcinoma breast like receptor status, BMI, lymphovascular invasion in both pre and post-menopausal women.

In this study the mean age of women with carcinoma breast was 48.57 years of age which is almost closure to Mehdi tazhibi et al study. In this study most of the patients were between 40 to 50 years which is similar to chopra et al study from Punjab. Thus most of the women with carcinoma breast are in their perimenopausal age.

In this study patient having BMI less than 25 were taken as normal and BMI more than 25 were taken as obese. We found that BMI is a statistically significant independent risk factor of carcinoma breast. In our study majority of carcinoma breast patients with ER +ve, PR +VE , BOTH ER & PR +VE have normal BMI, whereas the majority carcinoma breast patients with ER-VE,PR-VE, ER PR –VE status has BMI in obese range . This implies that patients with normal BMI has more chance for positive receptor status which has a better prognostic value whereas obese patients were associated with more negative hormonal receptor status tumour which has comparatively poor response to treatment. This observation is comparable to previous study from America, which analyzed breast cancer mortality in the obese group relative to the normal weight. In a study including African patients, overweight was significantly related to breast cancer mortality by multivariable analysis. However this study is controversial to Kawai et al reported that

obesity was an independent risk factor for breast cancer death but had no association with breast cancer prognosis.

We also correlate BMI with clinically palpable node. But there is no statistically significant association between node positivity and BMI.

In this study the lymphovascular invasion is more with obese (71.6 %), which is an independent poor prognosis for carcinoma breast. In our study the lymphovascular invasion is more in both pre and post-menopausal women and it is statistically significant ($p < 0.01$) which implies increased BMI as a significant risk factor in both premenopausal and post-menopausalwomen.This observation is similar to kang lu et al study in post-menopausal status but controversial to pre-menopausalstatus, which showed the following inference, that for premenopausal women, higher BMI could decrease breast cancer risk but higher BMI is associated with increased breast cancer risk in postmenopausal women.

In jain et al study 37.4% patients, had ER positive status and 62.6% patients had ER negative status while 34% patients had PR positive status and 66% patients had PR negative, whereas in our study we have the following observation 54% has ER receptor positive status , 60 % has PR receptor positive status. Among them 36.3% have both ER, PR receptor positive status. In our study we compared the Receptor status with BMI and lymphovascular invasion. Our study concluded that in patients having positive receptor status like ER+VE/PR+VE/ER & PR+VE, majority are in the range of normal BMI and has significantly lower lymphovascular invasion whereas in patients

having negative receptor status majority has lymphovascular invasion and has BMI in obese range.

This implies that positive receptor status is a good prognostic factor and chemotherapy can be effectively used as adjuvant therapy. This is comparable to the Dunnwald et al study, Vinita et al study which also concluded that ER/PR negative status has been associated with increased mortality.

Our study has 49.4 % HER 2 NEU receptor positive status which is comparable toJain et al study which has 35% positive status. There is no statistically significant association between HER2 NEU receptor status and lymphovascular relationship which is in contrast to Jain et al study.

Lymphovascular invasion is an important and independent prognostic factor of carcinoma breast. In our study 46% has lymphovascular invasion which was comparatively lower than young ju et al study. This may be due to larger sample study of that study. The lymphovascular invasion has statistically significant positive correlation with negative receptor(ER, PR, and ER&PR) status and BMI. But lymphovascular invasion was not statistically significant with HER 2 NEU and nodal status. This nodal status association is in contrast to young ju et al study.

CONCLUSION

CONCLUSION:

- Incidence of breast carcinoma is high in peri menopausal age group (40 – 50 years of age).
- In my study the following statistically significant results were obtained:
    - ❖ Positive receptor status(ER, PR AND HER 2 NEU) is found in majority of the women with normal BMI and negative receptor status is associated with obese patients.
    - ❖ Positive receptor status(ER, PR) are associated with decreased lymphovascular invasion and negative receptor status is associated with increased lymphovascular invasion.
    - ❖ Normal BMI is associated with decreased lymphovascular invasion in both pre and post-menopausal women in contrast to obese patients.
- Association of lymph node with lymphovascular invasion and body mass index is found to be statistically insignificant
- Association of HER 2 NEU with lymphovascular invasion is statistically insignificant.

LIMITATIONS:

- Our study involved only those women with carcinoma breast admitted in our surgical department; hence it does not reflect the data of the community.
- Our study doesn't include the patients with advanced carcinoma breast who were on neo adjuvant therapy.

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ANNEXURE

QUESTIONAIRE

PATIENT DETAILS:

Name: Age: Sex:

IP No:

ON ADMISSION:

Chief COMPLAINTS:

DURATION:

ASSOCIATED COMPLAINTS:

CLINICAL EXAMINATION:

Height: Weight:

Body mass index: [weight in kg/height in m2]

Pulse : BP :

RR : Temp :

Pallor: Icterus:

CVS: RS:

P/A: CNS:

EXAMINATION OF BOTH BREASTS:

EXAMINATION OF BOTH AXILLARY REGIONS:

INVESTIGATIONS:

LFT				
Total Bili				
Dir. Bili				
SGOT				
SGPT				
Total Protein				
Sr. Albumin				

HB%				
PCV				
TC				
RBC				
PLATELETS				
RBS				
Urea				
Creatinine				
Na^+/K^+				

CXR:

USG BREAST:

MAMMOGRAM:

USG ABDOMEN:

CT CHEST:

SKELETAL SURVERY:

BONE SCAN:

TRUCUT BIOPSY:

STAGE:

TREATMENT

OPERATIVE MANAGEMENT:

CHEMOTHERAPY:

RADIOTHERAPHY:

HPE REPORT:

FOLLOW UP:

INFORMATION SHEET

TITLE:**"A STUDY ON CORRELATION BETWEEN ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST"**

Name of Investigator :Dr.M.HARINI

Name of Participant:

Study Procedure: Patient will be subjected to clinical examination, routine investigations, X-ray, Usg Breast/Mammogram, USG abdomen, CT chest, skeletal survey/bone scan.

Possible Risks: No risks to the patient

Possible benefits

To patient: A better understanding of their problem so has to devise à plan of management which suits their needs.

To doctor & to other people: If this study gives positive results, it can help determine the prognosis of disease early which helps the doctor to plan the procedure correctly and their follow up with adjuvant systemic therapy. In future this will help in improving 10 year survival rate.

Confidentiality of the information obtained from you: The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time.Your decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator Signature of Participant

Date: Place:

PATIENT CONSENT FORM

Study Title : **"A STUDY ON CORRELATION BETWEEN ESTROGEN RECEPTOR, PROGESTERONE RECEPTOR, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS AND OTHER PROGNOSTIC FACTORS IN CARCINOMA BREAST"**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the Ethics committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms. ❑

I hereby consent to participate in this study ❑

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests and to undergo treatment ❑

Signature / thumb impression	Signature of Investigator
Patient's Name and Address:	Study Investigator's Name

NAME	AGE	IP NO	HEIGHT	WEIGHT	BMI	BMI (S)	MENOPAUSE	TUMOUR SIZE	NODE	ER	PR	HER 2 NEU	LYMPHOVASCULAR INVASION
Rajeshwari	45	1985	150	64	28.4	OBESE	NO	5*4	YES	NO	NO	NO	YES
bharani	49	11104	149	46	20.7	NORMAL	YES	5*3	NO	NO	NO	NO	YES
dharani	47	11701	160	70	27.3	OBESE	NO	4*3	NO	NO	NO	NO	YES
sokkubai	53	11976	158	56	22.4	NORMAL	YES	2.5*2	YES	YES	YES	YES	NO
nazir	55	12980	156	55	22.6	NORMAL	YES	2*2	NO	YES	YES	YES	NO
jayabala	45	12128	149	66	30	OBESE	NO	3*2	YES	NO	NO	YES	YES
devibala	35	11341	155	55	23	NORMAL	NO	2*2	NO	YES	YES	NO	NO
poongavanam	53	1113	160	58	22.7	NORMAL	YES	3*3	YES	NO	NO	YES	NO
panchavarnam	51	1163	148	60	27.4	OBESE	YES	3*2.5	YES	NO	NO	YES	NO
laila	37	11152	160	75	29.3	OBESE	NO	3*2	YES	NO	NO	NO	YES
pramila	35	12552	153	75	32	OBESE	NO	2*3	YES	NO	NO	NO	YES
pounammal	65	11306	160	76	30	OBESE	YES	5*2	YES	NO	NO	NO	YES
malliga	50	31306	150	68	30	OBESE	YES	4*2	YES	NO	NO	YES	YES
rose	53	32316	155	48	20	NORMAL	YES	2*4	YES	NO	NO	YES	YES
vasantha	45	11457	160	58	22.7	NORMAL	NO	4*4	NO	YES	YES	YES	NO
shobe	42	11472	155	56	23.3	NORMAL	YES	2*2	NO	YES	YES	YES	NO
manimala	40	12472	159	57	22.5	NORMAL	YES	2.5*2	NO	YES	YES	YES	NO
vanaja	48	14941	145	60	30	OBESE	NO	2.5*3.5	YES	NO	NO	NO	NO
radha	45	13941	150	68	30.2	OBESE	NO	3*2	YES	NO	NO	NO	NO
kalyani	34	11710	158	55	22	NORMAL	NO	4*4	YES	YES	YES	NO	NO
leelavathy	60	11736	160	58	22.7	NORMAL	NO	3*2	YES	YES	YES	NO	NO
santha	55	11760	155	78	32.5	OBESE	YES	4*4	YES	NO	NO	YES	YES
kasthuri	53	12760	162	60	23	NORMAL	YES	3*3	YES	NO	NO	YES	YES
sakkobai	53	11967	147	60	28	OBESE	YES	2.5*2	YES	YES	YES	NO	YES
subbamma	51	12957	160	58	22.7	NORMAL	YES	2*2.5	YES	YES	YES	NO	NO
jayabala	43	12128	148	70	32	OBESE	NO	2*2	YES	NO	NO	YES	YES
siva	41	12138	147	47	21.5	NORMAL	NO	3*2	YES	NO	NO	YES	YES
lakshmi	46	11633	152	78	34	OBESE	NO	4*2	YES	NO	NO	NO	YES

siva	45	11643	152	70	30.3	OBESE	NO	3*2	YES	NO	NO	NO	YES
indra	40	14136	157	75	30.4	OBESE	NO	5*4	YES	NO	NO	NO	YES
Ellamal	45	12015	158	56	22.4	NORMAL	NO	4*4	YES	YES	YES	YES	NO
vijayalakshmi	40	11221	145	40	19	NORMAL	NO	3*4	YES	YES	YES	YES	NO
Chellamal	42	12212	147	45	20.8	NORMAL	NO	3*3	YES	YES	YES	YES	NO
maliya	50	12780	163	60	22.6	NORMAL	YES	2*2	YES	NO	NO	NO	YES
gunasundari	52	12890	154	52	21.9	NORMAL	YES	3*2	YES	NO	NO	NO	YES
devi	40	11495	150	43	19	NORMAL	YES	3*2	NO	NO	NO	NO	NO
vani	42	11501	148	50	22.8	NORMAL	NO	2*2	NO	NO	NO	NO	NO
saraswathi	58	11502	149	65	29	OBESE	YES	2.5*2	NO	NO	NO	NO	YES
valar	56	12502	150	77	34	OBESE	YES	2*3	NO	NO	NO	NO	YES
ponni	55	12198	148	59	27	OBESE	YES	3*2	YES	NO	NO	NO	YES
kanmani	56	12287	162	60	23	NORMAL	YES	2*3	YES	NO	NO	NO	YES
chitra	40	13277	149	52	23.4	NORMAL	NO	4*5	YES	YES	YES	YES	NO
chinu	39	13371	157	55	22.3	NORMAL	NO	4*3	YES	YES	YES	YES	NO
lakshmi	45	12217	155	75	30.5	OBESE	NO	4*4	NO	NO	NO	NO	YES
maha	44	12397	160	75	29.3	OBESE	NO	4*3	NO	NO	NO	NO	YES
zubanth	50	11602	163	61	22.9	NORMAL	YES	3*3	YES	YES	YES	NO	YES
shivani	52	12701	158	54	21.6	NORMAL	YES	3*2	YES	YES	YES	NO	YES
jabin	38	11691	156	54	22.2	NORMAL	NO	3*2	NO	NO	NO	YES	NO
jaya	40	12691	160	57	22.3	NORMAL	NO	2.5*3	NO	NO	NO	YES	NO
malar	38	13681	160	77	30.1	OBESE	NO	3*3	YES	NO	NO	NO	YES
maya	39	13381	163	78	29.4	OBESE	NO	3*2	YES	NO	NO	NO	YES
kalaimani	47	13181	158	59	23.6	NORMAL	NO	3*3	NO	YES	YES	NO	NO
kala	45	13281	160	58	23.3	NORMAL	NO	3*2	NO	YES	YES	NO	NO
azizhuniana	65	11746	155	65	27.1	OBESE	YES	3*4	YES	NO	NO	YES	YES
amani	66	14746	150	48	21.3	NORMAL	YES	3*3	YES	NO	NO	YES	YES
banumathi	63	16746	156	76	31	OBESE	YES	5*2	YES	NO	NO	YES	YES
bhavani	65	17746	154	50	21.1	NORMAL	YES	2*4	YES	NO	NO	YES	YES

indhumathi	24	11861	158	70	28	OBESE	NO	4*4	YES	NO	NO	YES	YES
indhuja	30	15862	165	75	27.5	OBESE	NO	3*3	YES	NO	NO	YES	YES
lakshya	38	11884	145	45	21.4	NORMAL	NO	4*4	YES	NO	NO	NO	NO
elakya	40	12874	150	48	21.3	NORMAL	NO	3*4	YES	NO	NO	NO	NO
sarasu	50	11920	158	55	22	NORMAL	YES	3*3	YES	YES	YES	NO	NO
saranya	52	12930	159	69	27.6	OBESE	YES	3*2	YES	YES	YES	NO	NO
raghunathbee	65	11978	160	56	22	NORMAL	YES	3*3	YES	YES	YES	NO	NO
rhagavi	67	12977	161	58	22	NORMAL	YES	3*2	YES	YES	YES	NO	NO
yuvarani	70	12001	165	72	27.4	OBESE	YES	2.5*1.5	NO	YES	YES	NO	NO
yamini	72	14011	169	65	22.8	NORMAL	YES	2.5*2	NO	YES	YES	NO	NO
surya	50	12016	171	68	23.3	NORMAL	YES	2*1	NO	NO	NO	YES	NO
sandhya	52	12271	148	65	30	OBESE	YES	2*1	NO	NO	NO	YES	NO
banu	40	12317	156	58	23.8	NORMAL	NO	5*4	NO	YES	YES	YES	NO
mani	42	14316	154	52	21.9	NORMAL	NO	4*4	NO	YES	YES	YES	NO
sivali	40	12098	144	70	33.8	OBESE	NO	5*2	YES	YES	NO	YES	NO
sujeetha	42	13087	162	60	22.9	NORMAL	NO	4*2	YES	YES	NO	YES	NO
anwareshwari	53	11433	143	50	24.5	NORMAL	YES	4*2	YES	NO	NO	YES	YES
anjana	55	14432	149	65	29.3	OBESE	YES	3*2	YES	NO	NO	YES	YES
pachaiyammal	65	11437	150	50	22.5	NORMAL	YES	2*1	NO	YES	YES	NO	NO
priya	64	15437	158	55	22	NORMAL	YES	2*2	NO	YES	YES	NO	NO
sundarammal	45	11449	146	44	20.6	NORMAL	NO	2*2	YES	YES	NO	YES	YES
sundari	43	15449	148	57	26.7	OBESE	NO	3*2	YES	YES	NO	YES	YES
mahadevi	45	12111	158	55	22	NORMAL	NO	4*2.5	YES	NO	NO	YES	NO
mariyamal	44	13421	156	55	22.6	NORMAL	NO	3*3	YES	NO	NO	YES	NO
mathani	42	12421	154	70	30	OBESE	NO	2*3	YES	NO	NO	YES	NO
malini	45	11421	160	58	22.7	NORMAL	NO	3*2	YES	NO	NO	YES	NO
mary	60	11450	147	66	30.5	OBESE	YES	5*4	YES	NO	NO	YES	YES
mani	62	12454	156	66	27.1	OBESE	YES	3*2	YES	NO	NO	YES	YES
malika	58	13654	158	65	26.7	OBESE	YES	2*2	YES	NO	NO	YES	YES

gowri	39	12563	165	82	30.1	OBESE	NO	3*2	YES	YES	YES	YES	NO
ganga	38	12432	156	60	24.7	NORMAL	NO	2*3	YES	YES	YES	YES	NO
gayathri	36	13436	160	57	22.3	NORMAL	NO	3*3	YES	YES	YES	YES	NO
devi	57	12456	162	60	22.9	NORMAL	YES	4*3	YES	YES	NO	YES	NO
dhanya	55	16345	160	56	21.9	NORMAL	YES	3*3	YES	YES	NO	YES	NO
daya	54	14563	146	45	21.1	NORMAL	YES	4*3	YES	YES	NO	YES	YES
yazhni	53	15432	158	56	22.4	NORMAL	YES	4*4	YES	YES	NO	YES	YES
jayanthi	45	11200	149	47	21.2	NORMAL	NO	1.5*1	NO	YES	YES	YES	NO
jamuna	43	13478	165	63	23.1	NORMAL	NO	2*2	NO	YES	YES	YES	NO
janaki	47	12367	156	65	26.7	OBESE	NO	2*3	NO	YES	YES	YES	NO
sundaramal	60	11203	158	76	30.4	OBESE	YES	4*4	NO	YES	YES	NO	YES
soudamaal	62	12313	160	86	34.4	OBESE	YES	5*4	NO	YES	YES	NO	YES
santha	64	12431	158	54	20.4	NORMAL	YES	5*4	NO	YES	YES	NO	YES
sundari	76	11209	156	55	22.6	NORMAL	YES	5*4	YES	YES	NO	YES	NO
thilaga	73	12109	145	56	26.6	OBESE	YES	3*4	YES	YES	NO	YES	NO
thaiyalnayagi	70	12198	170	60	20.8	NORMAL	YES	4*3	YES	YES	NO	YES	NO
mahadevi	45	12176	143	55	28	OBESE	NO	3.5*3	YES	NO	NO	YES	NO
yuvashri	43	15476	165	60	22	NORMAL	NO	4*2	YES	NO	NO	YES	NO
nalini	47	15176	155	51	21.1	NORMAL	NO	3*4	YES	NO	NO	YES	NO
pattamal	38	11211	144	42	21.1	NORMAL	NO	3*4	YES	NO	YES	NO	NO
naveena	34	14156	146	65	30.5	OBESE	NO	2*3	YES	NO	YES	NO	NO
pavithra	36	13154	154	48	20.2	NORMAL	NO	3*3	YES	NO	YES	NO	NO
vanaja	48	11472	165	78	28.7	OBESE	NO	2.5*3	YES	NO	NO	NO	NO
vani	46	12474	155	68	28.3	OBESE	NO	2*3	YES	NO	NO	NO	NO
nalli	44	12574	155	64	26.6	OBESE	NO	3*3	YES	NO	NO	NO	YES
uma	42	16754	153	66	28.2	OBESE	NO	3*4	YES	NO	NO	NO	YES
shoba	42	13754	154	54	22.8	NORMAL	NO	3*3	NO	YES	YES	YES	NO
tamil	44	12756	157	55	22.3	NORMAL	NO	3*2	NO	YES	YES	YES	NO
udhaya	40	17546	154	62	26.1	OBESE	NO	3*3	YES	YES	YES	YES	YES

chinnamal	38	12171	163	61	23	NORMAL	NO	5*3	YES	NO	YES	NO	NO
magalam	36	13372	162	63	24	NORMAL	NO	3*3	YES	NO	YES	NO	NO
munjula	35	13272	155	65	27.1	OBESE	NO	3*2	YES	NO	YES	NO	NO
radhalakshmi	47	12243	154	62	26.1	OBESE	YES	3*2	NO	NO	NO	NO	YES
nagamma	49	13433	154	69	29.1	OBESE	YES	4*1	NO	NO	NO	NO	YES
rathi	45	12231	148	58	26	OBESE	YES	2*3	NO	NO	NO	NO	YES
meenathi	60	11258	155	65	27.1	OBESE	YES	4*4	YES	NO	NO	NO	YES
subulakshmi	63	11236	155	52	21.6	NORMAL	YES	5*2	YES	NO	NO	NO	YES
prema	62	12335	150	46	20.4	NORMAL	YES	4*5	YES	NO	NO	NO	YES
sandiya	34	80770	158	65	26	OBESE	NO	4*4	YES	YES	YES	NO	NO
mangai	38	80774	157	55	22.3	NORMAL	NO	2*3	YES	YES	YES	NO	NO
pushpa	36	81442	164	62	23	NORMAL	NO	4*2	YES	YES	YES	NO	NO
mariyammal	38	91276	164	70	26	OBESE	NO	4*3	YES	NO	NO	NO	YES
sadaiyammal	40	93276	160	70	27.3	OBESE	NO	3*2	YES	NO	NO	NO	YES
pangajam	36	94254	162	68	25.9	OBESE	NO	4*2	YES	NO	NO	NO	YES
latha	37	94354	154	54	22	NORMAL	NO	3*2	NO	YES	YES	NO	NO
madhu	35	94534	155	56	22	NORMAL	NO	3*3	NO	YES	YES	NO	NO
nandhu	39	94563	150	56	25	NORMAL	NO	3*3	NO	YES	YES	NO	NO
mainnala	53	95001	154	63	27.3	OBESE	YES	2.5*2	YES	NO	NO	YES	YES
pongudi	55	95050	158	66	26.5	OBESE	YES	4*1	YES	NO	NO	YES	YES
thaiyammal	54	95100	150	64	28.5	OBESE	YES	3*2	YES	NO	NO	YES	YES
jayaseela	55	95110	152	45	19.5	NORMAL	YES	1*2	YES	NO	NO	YES	NO
kavitha	60	96100	157	54	21.9	NORMAL	YES	3*2	YES	NO	NO	YES	NO
vijaya	57	96250	150	47	21	NORMAL	YES	2*3	YES	NO	NO	YES	NO
bharathi	55	96300	154	52	21.9	NORMAL	YES	3*2	YES	YES	YES	YES	NO
neela	53	96360	155	51	21.2	NORMAL	YES	3*3	YES	YES	YES	YES	NO
menaka	57	96340	158	55	22	NORMAL	YES	3*2	YES	YES	YES	YES	NO
kasthuri	45	97100	160	61	22	NORMAL	NO	3*5	NO	YES	YES	YES	NO
shanthi	49	97160	155	53	22.1	NORMAL	NO	2*4	NO	YES	YES	NO	NO

kamsala	**46**	**97180**	**153**	**60**	**25.6**	**OBESE**	**NO**	**4*3**	**NO**	**YES**	**YES**	**NO**	**NO**
arunkulai	**50**	**97300**	**154**	**61**	**26.6**	**OBESE**	**NO**	**3*2**	**NO**	**YES**	**YES**	**YES**	**YES**
anjalai	**52**	**97340**	**152**	**63**	**27.3**	**OBESE**	**YES**	**3*4**	**NO**	**YES**	**YES**	**YES**	**YES**
buvana	**48**	**97400**	**155**	**65**	**27.1**	**OBESE**	**NO**	**3*3**	**NO**	**YES**	**YES**	**YES**	**YES**
vatsala	**48**	**98410**	**154**	**60**	**25.3**	**OBESE**	**NO**	**2*3**	**NO**	**YES**	**NO**	**NO**	**YES**
shantha	**50**	**98450**	**147**	**64**	**29.6**	**OBESE**	**NO**	**3*3**	**NO**	**YES**	**NO**	**NO**	**YES**
riya	**46**	**98480**	**150**	**48**	**22.3**	**NORMAL**	**NO**	**3*2**	**NO**	**YES**	**NO**	**NO**	**YES**
indrani	**61**	**98900**	**150**	**49**	**22**	**NORMAL**	**YES**	**5*4**	**NO**	**YES**	**YES**	**NO**	**NO**
raljalakshmi	**51**	**98970**	**156**	**65**	**26.7**	**OBESE**	**YES**	**3*3**	**YES**	**NO**	**NO**	**YES**	**YES**
rathi	**55**	**99000**	**155**	**69**	**29**	**OBESE**	**YES**	**3.5*3**	**YES**	**NO**	**NO**	**NO**	**YES**
Rajeshwari	**62**	**99105**	**150**	**45**	**20**	**NORMAL**	**NO**	**3*1**	**NO**	**YES**	**NO**	**YES**	**NO**
sundari	**46**	**99200**	**160**	**55**	**22.5**	**NORMAL**	**YES**	**3.5*2.5**	**YES**	**YES**	**YES**	**NO**	**NO**
valliyammal	**62**	**99250**	**157**	**65**	**26.3**	**OBESE**	**NO**	**5*4.5**	**YES**	**NO**	**NO**	**YES**	**YES**
amudha	**39**	**99346**	**145**	**45**	**22**	**NORMAL**	**NO**	**4*4**	**YES**	**NO**	**NO**	**NO**	**YES**
santha	**55**	**99500**	**150**	**52**	**23.1**	**NORMAL**	**YES**	**4*4**	**YES**	**NO**	**NO**	**YES**	**YES**
Mani	**65**	**99510**	**155**	**70**	**31**	**OBESE**	**YES**	**5*3**	**YES**	**NO**	**NO**	**YES**	**YES**